DRUG UTILIZATION

A Comprehensive Literature Review

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LETTER OF TRANSMITTAL

The Honourable Murray Elston
Minister of Health
Province of Ontario
Queen's Park
Toronto, Ontario

Dear Minister:

We are very pleased to submit the enclosed Report on "Drug Utilization - a Comprehensive Literature Review".

The Report was prepared by the undersigned with the extensive research and editorial assistance of Mr. David Zakus, BSc, MES, a PhD candidate in the Department of Health Administration, Faculty of Medicine, University of Toronto.

While many people were involved in assisting with the assembling and analysing of the materials contained in the Report, the authors accept the sole responsibility for the interpretation and summation of the materials reviewed.

/dac
Encl.

Yours very sincerely,

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EXECUTIVE SUMMARY

An extensive review of the literature concerning prescription drug utilization from around the world was undertaken and reported on.

The problem associated with drug utilization involves both prescribers and dispensers, as well as consumers. From the prescriber perspective, there is little doubt that there has been and continues to be problems in prescribing.

The reasons for inappropriate prescribing have been identified to include the following:

a) inadequate training of physicians during their medical school.years and in the day-to-day application of drug knowledge;

b) inadequate sources of objective information available to practicing physicians about drug properties and indications;

c) the limited time available to practicing physicians to study and evaluate the therapeutic claims for newly marketed drugs;

d) the widespread custom of physicians to continue their drug education by relying mainly on the promotional activities of the drug companies; and

e) the exceedingly rapid turnover in the popularity of prescription drugs.

Among the strategies which have been identified in the report, the following most frequently appear in the literature as embodying the greatest potential for confronting the problems associated with inappropriate prescription drug utilization:

a) use of limited drug formularies;

b) substantial expansion of drug utilization review (DUR) systems;

c) use of educational techniques to influence prescribing, dispensing and utilization patterns;

d) introduction of innovative payment strategies to modify incentives for the prescribing and utilization of drugs;

e) encouragement of the development of alternative health care delivery systems which embody incentives to provide cost-effective services while ensuring continued access to quality health care;

f) encouraging the use of lower cost, generically equivalent products in place of no more effective but higher priced products; and

g) an effective linkage system between diagnostic and therapeutic data bases.

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ABBREVIATIONS

AAC - Actual Acquisition Cost

ADR - Adverse Drug Reaction

ASHP - American Society of Hospital Pharmacists

ATC - Anatomical, Therapeutic, Chemical Classification System

AWP - Average Wholesale Price

CME - Continuing Medical Education

COMPASS - Computerized On-line Medicaid Pharmaceutical Analysis and Surveillance System

DDD - Defined Daily Dose

DED - Defined Exposure Dose

DHSS - Department of Health and Social Services (UK)

DUR - Drug Utilization Review

EAC - Estimated Acquisition Cost

FMG - Foreign Medical Graduates

FPC - Family Practitioner Committee (UK)

FT10 - Prescription form from U.K.

GPEP - General Professional Education of the Physicians for the Twenty-First Century (Report)

HID - Health Information Design, Inc.

HIE - (Rand) Health Insurance Experiment

HMO - Health Maintenance Organization

HSO - Health Service Organization

ICD-9-CM - International Classification of Diseases, Vol. 9

IMS - Intercontinental Medical Statistics

JCAH - Joint Commission on Accreditation of Hospitals (USA)

LSAB - Pharmaceutical Data Ltd. (Sweden)

MAC - Maximum Allowable Cost

MEAC - Manufacturer Estimated Acquisition Costs

MHI - Mental Health Inventory

MIS - Management Information System

MMIS - Medicaid Management Information System

NDC - National Drug Code

NDTI - National Disease and Therapeutic Index (USA)

NHS - National Health Service (UK)

NPA - National Prescription Audit (USA)

OTC - Over-the-Counter

PAL - Prescription Advisory Leaflets

PAS - Professional Activity Study

PBS - Pharmaceutic Benefits Scheme (Australia)

PDS - Pharmaceutical Data Services (USA)

PIP - Pharmacy Incentives Plan

PMS - Post Marketing Surveillance

PPA - Prescription Pricing Authority (UK)

PPI - Patient Package Insert

PPO - Preferred Provider Organization

p.r.n. - When Required

P & T - Pharmacy and Therapeutics (Committee)

SIMS - Supplemental Information of Medication

VA - Veterans' Administration

WEAC - Wholesaler Estimated Acquisition Costs

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1. INTRODUCTION

1.1 Drug Utilization Review (DUR) - An Introduction and Overview

The safe and effective use of drugs is an exacting science. In an editorial in the Canadian Medical Association Journal, Mahon and Godden (1973) discuss the concept of therapy control. The major issues that they examine are: the widespread availability of drugs; the social acceptance of drug taking; the patient-physician interface; the expectation that a prescription for a specific drug or drugs will bring satisfaction to the patient; a health system that encourages a rapid turnover of patient visits; and the use of a prescription to terminate the visit.

As much as effective therapy is a goal of all health practitioners, it is nonetheless an elusive goal. Mahon and Godden go on to explain that this is the case because drug therapy is difficult to supervise outside hospitals, it is difficult to communicate effectively with many patients, there are limits to the individual physician's knowledge of the efficacy of commonly used drugs; and lastly, because therapeutics is still a relatively new science. Their suggestion for improvement is two fold: first, governments must devise a health care system that does not encourage overuse or misuse by increasing physician income based on the number of patients seen; and secondly, even though physicians select a drug for a patient, the patient must accept a share of responsibility for its use.

The widespread use of drugs is not unique to Canada or the United States. Binns (1974) writes in an editorial of the European Journal of Clinical Pharmacology of similar problems in Britain. He cites the tremendous cost involved but is more concerned with the potential for sub-optimal prescribing leading to inadequate treatment or unnecessary side-effects. The problem raised is physicians' limited knowledge of the drugs available to them. The suggestion is put forward that it should not be so difficult to achieve better utilization of drugs as it is only a small number of drug entities that account for a high proportion of prescriptions.

The consumption of drugs is the result of drug-giving by health care providers and drug-taking by consumers. The rate and duration of drug consumption is dependent upon many factors. Among these factors are a) prescribing, whether appropriate or not; b) dispensing behaviour of pharmacists; c) administration of drugs by nurses; and d) self-selection and ingestion by patients, i.e. self-medication. There is always the need to question drug use, and in particular, whether drugs are being used in a rational and effective fashion.

The need for reviewing drug use has been pointed out by Rucker (1970) based on a desire for more rational prescribing. Such a review finds usefulness in that its primary purpose, patient care, is given priority attention, and problems of over and under-prescribing as well as mal-prescribing are addressed. He indicates that "successful drug utilization review programs are likely to be characterized by local implementation, the establishment of effective standards to minimize irrational prescribing, the use of voluntary techniques to attain more rational use of drugs, and the adoption of an impersonal approach to problem solving."

It becomes important to differentiate between "drug surveillance" or "drug monitoring", and "drug utilization" or "drug use." The former terms seem to be more concerned with the clinical effects of drugs, and the latter terms with identifying the drugs that are used in a particular environment (Miller, 1974). Stolar (1978) offers an operational definition of DUR studies and programs by differentiating them into quantitative and qualitative studies. Quantitative studies are those concerned with "quantifying various facets of drug use within a health care system" such as a hospital, nursing home, or health insurance plan. Data are collected, organized and displayed as estimates or measurements of drug use for a defined time period, drug, patient or prescriber. These data are used for making financial decisions such as preparing drug budgets. Qualitative studies are "multidisciplinary operations which collect, organize, analyze and report information on the rationality of the drug use base" and "are generally one-time examinations of narrowly defined areas of drug use." This type of study usually includes the concept of criteria or "predetermined elements against which aspects of the quality, medical necessity and appropriateness of medical care (e.g. drug use) may be compared."

Stolar (1978) describes a DUR program as:

> an authorized, structured, ongoing system for improving the quality of drug use within health care organization by evaluating it using predetermined standards and initiating efforts to correct patterns of drug use which are not consistent with these standards. It includes a mechanism for measuring the effectiveness of these corrective actions.

It then becomes a way for assuring the quality of drug use.

The process of DUR, thus, requires structure. Brodie (1972) has considered this in some detail. In order to standardize the way in which a DUR is conducted, he has put forward a number of definitions taken from the literature:

a) Utilization Review: a study of the frequency of charges or services to determine patterns of service or charges.

b) Peer Review: a review of the quality of care provided a patient including documentation of care (medical audit), diagnostic steps used, conclusions reached, therapy given, appropriateness of utilization (utilization review), and reasonableness of charges (claims review).

c) Drug Utilization: consists of the prescribing, dispensing, administering and ingesting of drugs.

d) Drug Utilization Review: the ongoing study of the frequency of use and cost of drugs, from which patterns of prescribing, dispensing, and patient use can be determined.

"The goal of drug utilization review is to improve the quality of patient care through the prescription and the use of appropriate drugs in conditions for which their use, based on sound medical judgement, is indicated and at a minimal cost consistent with an acceptable quality of care. The process for attaining this goal is education" (Brodie, 1972).

An ideal DUR program should provide four profiles on a continuing basis and at predetermined intervals. These profiles are that of the drug (therapy), patient (diagnosis), physician (prescriber), and pharmacy (dispensing record). Finally, Brodie pinpoints the need for automation based on volume of data. It would also seem apparent that speed of manipulation and accuracy of data handling are also advantages of automation.

The considerations of cost (relative to patient care) and the concept of linkage (linking diagnosis and other medical data to the drug review) become important. The traditional view of DUR held by third party payors that is overwhelmingly directed toward fiscal control and fraud detection, overlooks the more important aspect of quality assurance of therapy. Certainly, the priorities must be reversed if DUR is to be meaningful to health care providers.

Although operational and standardized definitions are useful in running a drug use review program, a certain amount of flexibility in the system is required. The importance of this flexibility is stated by Huber and Patry (1981) who suggest internal standards be used. They are of the opinion that these enhance the use of standardized criteria and will then allow comparisons of data among various sites.

The outcome of DUR is to reduce the incidence of drug therapy failure and drug induced illness. In short, it is to encourage and achieve rational, safe, and effective drug use at a reasonable cost.

Morse et al (1982) define some specific objectives to prevent the following: underutilization, overutilization, iatrogenic effects, adverse reactions, contraindicated combination use, and drug therapy contraindicated by diagnosis.

Drug use review, as the literature sets out, is a task to be dealt with seriously. In the United States, hospitals must perform reviews if they wish to maintain their standing with the Joint Commission on Accreditation of Hospitals (JCAH). Skilled nursing facilities receiving Medicare reimbursement must meet federal requirements that include DURs. Medicaid state plans require such reviews in intermediate care facilities as well.

Behling (1981) provides an explanation and outline of the quality assurance standards of the JCAH. In short, they are:

a) Quality assurance is the responsibility of the institution's governing body.

b) Quality assurance programs should be systematic and ongoing, and all such activities in the institution should be coordinated to avoid duplication.

c) The quality assurance plan must be written. It should be a working document and need not be complicated. It might be no more than an organizational chart that describes reporting methods and tells who is responsible for what.

d) Physicians and other health care professionals should participate in the quality assurance program.

e) The program must focus on known or suspected problems and must be based on predetermined, clinically valid written criteria. But no specific methodology is required.

f) Appropriate action should be taken to eliminate identified problems and there should be follow-up to assure that that action was effective.

g) Program findings need to be reported to the medical staff, governing body and chief executive officer as appropriate.

h) Quality assurance activities should be reviewed at least annually.

The review of pharmacy and therapeutics within an institution is also outlined in the JCAH standards:

"The development and surveillance of pharmacy and therapeutics policies and practices, particularly drug utilization within the hospital, shall be the responsibility of the medical staff and shall be carried out in cooperation with the pharmacist and with representatives of other disciplines as required...Written reports shall be maintained that reflect the results of all evaluations performed and actions taken. Individuals charged with these responsibilities shall, in an ongoing manner, advise the medical staff and the hospital's pharmaceutical department/service on matters pertaining to the choice of drugs available for patient care and diagnostic testing, and on the addition or deletion of drugs in the hospital formulary or drug list. The responsibilities of individuals performing the pharmacy and therapeutics function also shall include the development of a formulary or drug list,... the review of all untoward drug reactions, and the evaluation and approval of all protocols concerned with the use of investigational or experimental drugs...The pharmacy and therapeutics activities shall be performed at least quarterly and documented" (Behling, 1981).

The JCAH standards also outline antibiotic use review. Such a review "should include review of the prophylactic use of antibiotics for inpatients, and ambulatory and emergency care patients. Criteria for the prophylactic and therapeutic use of antibiotics should be established in problem areas, and departures from these criteria should be reviewed in a timely manner...Care must be taken to assure that assessment includes a clinical review as well as any statistical/prevalence study of antibiotic usage. Both susceptibility/ resistance trend studies performed in conjunction with the infection control function, and pharmacy-oriented statistical/prevalence studies may serve as information bases from which more specific assessments may be performed employing suitable criteria for the use of the specific antibiotics involved" (Behling, 1981).

Third party payors or fiscal intermediaries can play in important and useful role in DUR. As has been mentioned, the basic interest of these fiscal intermediaries is financial control. Usually, this is accomplished by claims review, administrative screening review, and recently by introducing professional review mechanisms to control drug use (Jinks and Hirschman, 1978). Administrative screening involves quantitative criteria that limit cost per month, claims per month, claims within the same therapeutic class per month, and number of providers accessed by the patient per month. Professional review, on the other hand, is accomplished by using professionals to render opinions on claims that fail administrative criteria and may include such guidelines as dose limits or duration of therapy.

Lastly, peer review is important; defined here as "a hierarchial system of specialists (e.g. pharmacists) who study data, investigate professional patterns which vary from the usual, and communicate the results of their investigation and recommendations to their peers with the view of sharing valuable information about the health status of the community, and of individual patients" (Jinks and Hirschman, 1978).

Because of the data base collected and retained by fiscal intermediaries, there is opportunity to exploit it beyond simple clerical tasks. The opportunity occurs at an ambulatory level where pharmacists, preferably who have specific training, can use the data to interact with patients and physicians with a view to changing expectations about drugs, irrational prescribing, drug interactions, and compliance. A problem remains, however. Simply, it is the lack of a total patient drug history that can be shared by pharmacist and physician before drug related decisions are made. Potentially, the use of interactive computers will help to solve this problem in the near future.

As the advantages of DUR become more widely accepted among health professionals and researchers, a number of models have begun to emerge. Stolar (1977) has devised a conceptual framework for drug use review, medical audit, and other patient care review procedures. He illustrates the 'quality assessment form' developed by the American Society of Hospital Pharmacists as part of a model established for outpatient prescription services. The form allows model criteria to serve as a starting point for criteria development. As a result, the pharmacist's role becomes defined in the overall quality assurance program of the hospital, with specific emphasis on drug use review and quality assurance of pharmaceutical services.

Recently, provincial drug benefit programs have become interested in using the data accumulated through providing and paying for drugs to eligible recipients. One example is in British Columbia (Hlynka and Danforth, 1981). A complete DUR program was designed and implemented. Two projects were undertaken: one to review selected drug usage among the ambulatory population who received drug benefits; and one among long-term care patients. Suspected problems were identified, corrected through an educational program, and a follow-up review performed.

In this program, there was a high degree of cooperation among the provincial program administrations, the College of Pharmacists, and the College of Physicians and Surgeons. it was this cooperation that played a large part in the overall success of the program and seems to demonstrate the need for linkage among providers and agencies.

The importance of data linkage is illustrated by Knapp et al (1977) and Gross (1981). They explored whether or not the addition of diagnosis or intended drug use information would improve the drug use process sufficiently to warrant extra effort in obtaining such information. They found that it was possible to link these data in about 90% of all prescriptions dispensed. The biggest difficulty, according to these researchers, was the lack of specificity in the information provided by prescribers. As a result, they recommend that unless the diagnosis or intended use of the drug can be validated, it may not be useful.

Because provincial health care plans reimburse any one of the physician, pharmacist or patient, it can be speculated that fairly accurate data are collected before payment is made. The resulting data banks should therefore afford ample data and linkage opportunities for meaningful DURs. The role of the computer in the DUR process is discussed by Rucker (1972).

He distinguishes among retrospective, prospective, and concurrent reviews. Because of time delays with retrospective reviews, there are advantages to be gained with prospective and concurrent reviews. It is in these instances where the use of computers is helpful.

In order to conduct a DUR, Tremblay (1981) indicates that an appropriate climate is needed. He explains that objectivity, neutrality, and confidentiality are essential for a successful program. In meeting these criteria, a climate conducive to learning is achieved implying the absence of punitive action. Rather, the strategy for intervening in a positive way is that of education.

DUR methodology is set out by Knapp and colleagues (1974) where they stress the importance of developing and applying criteria. They illustrate the usefulness of this approach with a sample set of criteria along with sample data and analysis for one type of DUR.

The need for uniform data is explained by Forbes et al (1981) in the context of hospitals. The researchers bemoan the fact that there are no nationwide (U.S.) data available on key elements of drug use and prescribing. The problem identified here is one of lack of uniformity in recording drug information. They present a table listing advantages and disadvantages of various types of hospital data and their respective sources. In addition, there is a proposed data collection form suggesting a minimum of data elements that should be collected for all records.

A DUR model was constructed by Brodie and Smith (1976), and its application in a hospital is discussed by Brodie, Smith, and Hlynka (1977). They suggest that five components are required: authority; operational and demographic characteristics of the delivery system and the population served; the existing profile of drug usage; standards of appropriateness in order to judge drug usage; and a scheme of evaluation to measure the impact of review.

From the above model's criteria, a drug use review program when implemented judiciously should be able to achieve the following goals: a) an improvement in the level of patient care and often a reduction in the cost of care; b) an improvement in the management and utilization of hospital resources; c) an improvement toward clarification of the drug component of patient care, and better integration of pharmaceutical services with other hospital services; and d) an improvement in the fact-finding capacity that can contribute to both the identification of need for and implementation of hospital programs.

Because the conditions for participation in the Medicare and Medicaid programs in the United States require that a pharmacist be responsible "for developing, coordinating, and supervising all pharmaceutical services" in long-term care facilities, it is imperative that a system be established to accomplish this. Brodie, Lofholm, and Benson (1977) have suggested a model for a Skilled Nursing Facility.

If the pharmacist is to be actively involved, he/she must be familiar with the mandated requirements, understand the characteristics of nursing home patients, understand the drug use process in the homes, and be familiar with the medication needs of these patients. One problem that occurs is the lack of an organized medical staff and limitations of support services for a review to take place.

The authors indicate, however, that a Pharmaceutical Services Committee can assume the responsibility for setting and maintaining drug use standards. The conceptual DUR model can be adapted to these facilities by developing and using monthly patient review data.

Another approach to DUR is to use a Professional Activity Study (PAS) system as described by Hoffmann (1979) with suggestions for implementation. PAS originated in the early 1950's through a grant by the W.K. Kellogg Foundation for a study of professional activities in hospitals. Its major advantage is a standardized procedure of data collection allowing comparisons among institutions. It is also noteworthy because Canadian hospitals participated.

Briefly, PAS involves completing an abstract for each discharged patient. The data are computer analyzed and the results are available to administrators and others who use them in planning and managing the hospital, and evaluating quality of care. In addition, drug usage information is available for 12 different drug types and is adaptable to utilization review on the following areas: drug type, diagnosis, routine investigative patient data, and quality assurance review of drug therapy.

Hoffmann (1980) provides an illustration of PAS for drug use review in a retrospective trial audit. He provides a schematic of the process and cites three advantages of the method: a) many hospitals already utilize the system; b) specially oriented medical records personnel can collect the necessary data without much additional effort; and c) a variety of retrospective drug audits can be conducted in an ongoing manner with appropriate direction and coordination.

Other examples of DUR appear in the literature. Among them, a program using the Pharmacy and Therapeutics Committee (Anon, 1977), and another that uses medical record technicians and an abstracting service format that is claimed to be both efficient and economical (John and Spieler, 1981). Gregory and Knapp (1976) reviewed 22 DUR studies published between 1970 and 1975 in sixteen journals in an attempt to assess the current state-of-the-art. They judged these studies based on norms, criteria, and standards.

Their results indicate the studies to be, in general, inefficient, using implicit criteria leading to unreliable reviews, because of judgemental and subjective decisions rather than objective decisions from explicit criteria. They also note that most studies were retrospective, thus not benefitting patients immediately, that antibiotics were most frequently studied ignoring other important classes of drugs, and that follow-up of prescription feedback was lacking.

An example of a manual approach to DUR is provided by Kelly, White, and Miller (1975). They conducted a program in a community hospital, claiming it to be simple as it only takes three or four hours a month of a pharmacist's time. It also involves nurses, physicians, the drug information service, and the medical records librarian. Other advantages cited are its on-going nature and effectiveness as it achieves desired results of improved patient care. Other examples include one by Dancey (1978) who reports a DUR study in a general hospital in Vancouver, and one by Zilz (1978) in Wisconsin.

The call for continued work in this area is made by editors of professional journals, in particular the pharmacy literature. In a 1973 editorial in the American Journal of Hospital Pharmacy, Provost (1973) called attention to the guidance needed from organized hospital pharmacists for individual hospital pharmacists to institute DUR programs. These sentiments were echoed by Summers (1978) writing in The Canadian Journal of Hospital Pharmacy, and by Zilz (1976) in the American Journal of Hospital Pharmacy who also points out the importance of involving pharmacists in the process.

Not to be left out of a literature review of this area is the cost of conducting DURs. One approach that examined this aspect is reported by Knapp and Palumbo (1977). This particular study involved the manual collection of data using a sampling procedure; application of dosage, therapy length and drug diagnosis screening criteria; sorting and tabulation of data by computer; and analysis and reporting of the summarized data. The areas of direct costs were identified as: a) development of criteria; b) computer programming; c) data collection; d) data coding and processing; and e) data analysis and reporting. It is also important to note that other costs occur such as time spent by involved health professionals and may represent hidden costs of the process.

Other studies have looked at DUR programs with the specific purpose of decreasing drug cost. Basically, two strategies are used: restricted drug use controlled by a formulary (Blaufuss, 1981); and less expensive alternative drugs or therapies (Hoffmann, 1984).

1.2 Drug Use - Too Much or Too Little?

The question of "how much drug or drugs is enough?" is not one that is answered easily. The literature provides a picture of drug use taking in all facets of demography, practice sites of health care providers, institutional and ambulatory patient settings, and private as well as public programs. What emerges is a diverse description of drug giving and drug taking with a common theme - the need and desire for rational and appropriate use of drugs at a reasonable cost.

Stating that "America is an overmedicated society", Lee (1980) provides a working definition and data to build his case. Prescription drug sales in the U.S. have grown at a steady rate reflecting increased drug use. This is substantiated by a growing increase in prescription volume. Lee contends that this has led to an 'overmedicated society'.

Essentially, overmedication exists when drug use is either unjustified or inappropriate. Use is unjustified when there is no proper indication for the drug or when the drug is ineffective.

Inappropriate drug use occurs when more effective or less hazardous drugs are available, when a drug is used in excessive amounts or for an excessive length of time, and when a fixed combination drug is used when only one of the components is indicated. Lastly, inappropriate use occurs when a costly drug is prescribed and a less costly one of equal effectiveness is available.

At the same time, Lee recognizes that some patients are undermedicated, that some hospitalized patients suffer severe pain and are given inadequate relief, and that many depressed patients are under-treated or untreated. This in no way balances out inappropriate and unjustified drug use, and the problem of overmedication still exists. Certainly, more research is required in order to define, understand, and solve this problem.

Rabin (1972) has examined the literature concerning the use of medicines both prescribed and nonprescribed. His paper indicated that the literature was modest in size and related mostly to the use of prescribed medicines. Cross-national, national, and local studies all indicated that considerable variation existed in the ratio of prescribed drug use among different populations. Rabin suggested that the differences in drug use rates were dependent upon cultural factors that characterized the different populations, and upon professional factors relating to their physicians. It appeared that female gender, higher education and social status, low and high income range, older age, and greater mobility all tended to be associated with increased drug use. Psychotropic drugs such as sedatives, tranquilizers, hypnotics and stimulants were the most commonly prescribed, followed by anti-infectives. Prescribing rates were largely determined by the physicians in a given area; and among them, specialty was an important determinant.

Less is known about non-prescribed drugs. However, what little information is available in the literature points to analgesics being the most commonly purchased and consumed.

Rabin and Bush (1974) later completed an historical review of current levels of drug consumption. Basically they found that medicine use has increased worldwide at rates exceeding increases in national incomes in most countries.

The use of medication may be an indicator of health status and medical practice in defined populations. The relationship between drug use and physician use appears to be a rather strong one. Kasper and Wilson (1983) examined this issue based on data contained in a 1977 report. They found that children from poor and less educated families have less likelihood of receiving a prescription than do better off children. The difference, according to the authors, appears to correspond to levels of physician use. However, when poorer children did see a physician, there was no difference in the number of prescriptions written for them; simply indicating a similar physician response to childhood illness regardless of patient's social class. In general, the differences in access for older persons were not observed regardless of income or education. The elderly poor, however, required more prescriptions than the better-off.

If the majority of drugs are obtained by prescription, the question of how many prescriptions go unfilled is one of interest. One report (Anon, 1982) indicates that up to 20% of patients receiving a prescription in general practice in Britain do not get it dispensed. This failure is apparently due to the following factors: a) poor discussion and lack of information; b) mistaken beliefs about drugs; c) failure of a physician to understand or identify the major reason of a patient visit; and d) simply that many patients do not expect a prescription.

In fact, there was a time when the prescription was a fairly private matter involving physician, patient and pharmacist (Wertheimer, 1983). This is no longer the case. Curiosity and technology have changed that. As the prescription became recognized as a useful and important source of information, it was and is used for insights into prescribing, decision making, compliance, and other behaviours. The role of the prescription in therapy was explored by Hemminki (1975) who questions the importance placed on medication in treating all patients.

It seems that patients vary from the one extreme, of not having a prescription dispensed, to the other of actively seeking out prescriptions from one or more physicians. The extent of drug use, in particular inappropriate drug use, is exacerbated by the phenomenon of polypharmacy. The belief that if one dose is indicated, two or three might be that much better is often followed by patients with multiple symptoms, multiple physicians, and misinformation. The causes, consequences, and cures are discussed by Kroenke (1985). Two other examples of polypharmacy deal with computer feedback used to alter prescribing habits (Barton, 1978) and the incidence of polypharmacy in psychiatric treatment (Sheppard et al, 1969).

With the advent of increasing drug use, it is expected that governments should become interested for several reasons. The first cause of concern is public safety and rational drug use; the second is cost, in particular where governments are a major purchaser or payer of drugs.

Henderson (1976) outlines governmental concerns as the following: overprescribing; inappropriate prescribing; drug toxicology; excessive costs of medication; morbidity and mortality from traffic accidents secondary to drugs; and the present lack of mechanisms of review or control by provincial or national medical associations of a physician's competence to prescribe. As well as indicating these problems, he suggests some mechanisms to achieve improvement in the environment. For example, the use of prescribing profiles and regular peer review of them, continuing education, and improved drug information systems.

Muller (1972), considering the marketplace forces that influence the degree of medication use, and indeed overmedication, suggests ways to modify drug use. She is of the opinion that "imposing some constraints on the behaviour of drug companies and other participants in the medical care market and attempting to exert a long term influence on the relative desirability of the various options open to doctors, hospitals, patients, pharmacists, and suppliers of drugs" is required. She further states that "a review of drug utilization is another device that can be used, either to supplement a formulary or as an independent means of achieving rational prescribing; qualified professionals would evaluate the prescribing done by individual physicians on the basis of scientific standards." Muller then continues to describe briefly the process involved.

The need for objective review and assessment of drug therapy is unquestioned. What remains, however, is how to conduct it with a minimum of interruption to the delivery of health care and inconvenience to the providers and consumers, and at a reasonable cost. The literature review that follows is an attempt to describe how this might be accomplished.

2. SOURCES OF DATA, SYSTEMS AND METHODS REVIEW

Sources of data for drug utilization will be reviewed within three broad areas, namely: a) the general principles underlying the type and quality of data required to conduct any DUR; b) hospital or institutional DUR; and c) those broad national, regional or international systems which have been developed for the express purpose of assessing drug utilization epidemiology.

2.1 General Principles

a) Drug: A review may consist of all drugs, a group of drugs or an individual drug or product. Studies of drug groups should be clearly defined, using if possible a well-accepted classification, such as that of the American Hospital Pharmacists Association or the Nordic Anatomical/Therapeutic/Chemical (ATC) system.

b) Country: The interpretation and application of DUR data should define the country of countries involved such that the reader may interpret the data in the light of any national regulations or restrictions which apply to particular drugs or health care systems.

c) Region: The demography of a region may make it particularly useful to sample the DUR pattern of a country. However, there is a risk that a region, once representative of a country or group of countries, may become unrepresentative as a result of the DUR process itself.

d) Pharmacy: Information derived from the process of drug supply may be used to study utilization. The retail or hospital pharmacist has the most immediate contact with the patient. Less reliable information may be obtained from a drug distributor, a drug importer or a drug manufacturer. The value of these alternative sources depends on whether or not the national environment permits single or multiple sources, and on the presence or absence of legislation controlling the confidentiality of the source information.

e) Insurance System: The system of medication insurance may be a valuable source of information concerning drug utilization. Constraints on confidentiality and the choice of drugs, or the eligibility of patients for benefits by age or economic status may influence the comparability of data.

f) Institution: In general, institutional data provide a reliable source for drug utilization review, but the age of patients, nature of disease, level of care, and the presence and nature of a formulary system may have serious impacts on the comparability of data.

g) Physician: Knowledge of the status of physicians by location of practice (e.g. hospital, family, or public health), age, time since qualification, and other demographic data such as nature of practice, country of graduation, and training in other countries can help in the interpretation of DUR data.

h) Patient: It is important to know if the data collected from patients have been obtained from a survey or questionnaire or if they have been obtained directly from prescription originals or duplicates. Since the provision of a prescription does not necessarily guarantee that the patient takes the drug, a measure of compliance can be useful and may include an analysis of drug effect or blood level. The distribution of patients by sex and age should be known. Other aspects such as race or socio-economic status may be relevant to the applicability of data to other patient groups.

i) Indication: Ideally the process of DUR should include a link with the disease, so that the appropriateness of therapy can be assessed and possible associations with adverse effects can be identified.

j) Unit of Drug Measurement: International differences in availability of individual drugs and monetary exchange rates may make it difficult and inappropriate to compare costs. The Defined Drug Dose (DDD) has evolved as a useful measure of quantity which permits an effective comparison of prescribing patterns for classes of drugs, even when individual drugs within that class differ from country to country. Alternatives to the DDD include the Defined Exposure Dose (DED) which will also be discussed more fully later.

k) Accessibility of the System: Knowledge about accessibility to a particular system is useful if the data are to be applied to answer questions raised by investigators outside the system.

1) Structure of the System: Information regarding the facility, investigators and other personnel, equipment and programs permits an evaluation of the competency and cost-effectiveness of the system itself.

2.2 Hospital DUR

The hospital-based DUR is an important process for evaluating proper drug choice, fiscal pharmacy management, physician education and hospital accreditation. DUR may be conducted in a retrospective, concurrent or prospective manner.

In the retrospective process it is usual for a DUR pharmacist to be designated as project coordinator with assistance from appropriate physicians and record staff. A review of drug utilization and expense is conducted to identify high volume, ineffective, potentially hazardous or costly medications in which changes in prescribing patterns may have efficacy, safety or financial implications.

Usage criteria are established on the basis of expert opinion. Alternative therapies are identified and criteria for appropriate substitution are developed and incorporated into usage criteria. Local review by medical staff is undertaken to determine if the criteria are useful. It is then appropriate for the Pharmacy and Therapeutics (P&T) Committee to review and approve the criteria and for the Medical Audit Committee and Records Committee to approve the nature and process of the audit. Subsequently, the Medical staff are informed of the criteria.

Data are collected and opportunities for alternative therapies are noted. Data analysis is undertaken to determine cost savings if proper drug utilization and alternative therapies are to be implemented. Cost savings due to proper drug utilization and alternative therapies are expressed in terms of potential annual savings. A process of active education of medical staff on drug utilization, alternative therapies and potential savings is then undertaken. A follow-up review is also conducted to assess the success or failure of this educational intervention. If education has not been successful, modification and repetition of active interventions and assessments are instituted. The results of the DUR are reported to pharmacy, nursing and medical staff to reinforce changes in prescribing habits.

In a prospective or concurrent process, usage criteria are developed as described earlier. The pharmacy staff identify the orders for specific drug usage and alternative therapies. The DUR pharmacist receives all drug orders for the drug under review and compares the prescribed therapy against usage criteria. When prescribed therapy does not coincide with the approved usage criteria, the prescribing physician is contacted and asked to alter the order. The physician may or may not accede to this request and is responsible for the final decision. Subsequently, the impact of DUR is assessed by examining utilization and costs before and after intervention. Cost savings are expressed on an annual basis. The results are then disseminated to the appropriate hospital staff.

2.3 National and International Systems

2.3.1 Canada

The **British Columbia** Pharmacare prescription drug care program was initiated by the B.C. Ministry of Human Resources in 1974 (Hlynka and Danforth, 1981; Danforth et al, 1982). The program was developed with several specific objectives. They were: a) to identify potential problems of target drug usage among ambulatory and long term care patients as determined from Pharmacare prescription records; b) to verify and correct any problems identified through practicing physicians and pharmacists; and c) to assess the effect of the corresponding corrections by comparing the incidence of potential problems between pre and post-education periods.

Computerized prescription records are based on monthly billings as submitted by participating pharmacies. The corresponding information made available for DUR includes the identification of a patient, prescribing physician, dispensing pharmacy, drug quantity, cost, prescription number and date filled. Computer programs were designed to enable this data to be retrieved in any combination according to the requirements of specific measurement criteria selected for DUR.

Based on the philosophy that DUR should be controlled by the professions responsible for prescribing and dispensing drugs rather than by the sponsors paying for them, a professional review committee was structured to assume general responsibility for the B.C. program. Representatives from the College of Physicians and Surgeons and the College of Pharmacists of British Columbia were appointed to the committee to serve as the professional authority in this respect. These members approve the choice of target drugs and measurement criteria proposed for review and arrange for corrective procedures to be employed in dealing with any problems identified. The manager of Pharmacare represents the sponsor's interests and provides the financing necessary for research costs related to data retrieval and analysis.

A research team made up of pharmacists with varying research and clinical backgrounds serves as the program's research intermediaries. In addition to designing the research protocols for DUR, proposing the parameters to be considered for each specific study and retrieving and analyzing the corresponding data, the intermediaries perform important roles in providing an unbiased interpretation of the results and ensuring confidentiality.

The integration of the data base for virtually all components of health delivery is the nucleus of the **Saskatchewan** system. Hospital care, ambulatory care, vaccination programmes, cancer clinics and drug use can be investigated through the cooperation of statisticians and health professionals (CMAJ, 1980). Over-the-counter (OTC) and non-formulary prescription medications are not health benefits and are, therefore, not documented. Applications of the program include the evaluation of patterns of prescribing for the elderly in Saskatchewan in 1976 (Skoll et al, 1979).

The Manitoba Health Services Commission (MHSC) maintains a master registry of the population and well documented claim files for hospitals, physicians, and personal care (nursing) home services (Mossey et al, 1981). The provincial Office of Continuing Care maintains files for home care use. Since Manitoba's Pharmacare Plan offers partial reimbursement to individuals or families whose annual prescription drug costs are more than $50.00, each application for Pharmacare benefits provides specific information on the type, amount and cost of all prescribed drugs, as well as the route of administration and duration of therapy. Heavy drug use among the elderly has also been surveyed in Manitoba (Mitenko et al, 1983).

2.3.2 United States of America

Data bases on prescription drug use in the USA are reviewed by Kennedy (1978). There are at least two major sources of this type of information in the private sector. One potential source is International Medical Statistics (IMS) America, a multinational information gathering organization. It regularly prepares reports on the patterns of drug use in the United States. In addition, IMS America obtains information on the incidence of disease in the United States and the medical treatment used for these diseases. The U.S. federal government purchases some of the services of IMS America, but these information banks are not readily accessible to researchers or to the public.

Another particularly interesting data base is the National Disease and Therapeutic Index (NDTI). The NDTI obtains information from a statistical sample of office-based physicians in the United States who periodically report on their own behaviour in diagnosing and treating patients. From the survey, one can obtain information such as how many patient visits in the United States occur for a particular disease over a period of time and how that disease is treated.

A second type of data base which is capable of describing how prescription drugs are used is found in the computer banks of organizations which process payments for prescription drugs. These organizations process claims for programs such as Medicare and Medicaid, and for unions or other organizations which pay for their constituents or employees.

It is suggested that use of Medicaid prescribing data can be an efficient and accurate way of conducting large scale surveillance of mis-prescribing and of targeting interventions that can improve sub-optimal drug utilization (Ray et al, 1985a and 1985b). In a follow-up period the same data can be used to monitor the effectiveness of each mode of intervention and measure the degree of behavior change for each physician. The authors comment that the quality and reliability of data systems vary widely. Some states have progressed well in the development of systems. They commented that states are increasingly broadening the purposes to which their Medicaid

Management Information System (MMIS) data can be put. The MMIS is a computerized claims processing and management information system created in 1972 by the U.S. Department of Health, Education and Welfare for fiscal and administrative control of Medicaid. One major advantage of the MMIS data set for drug utilization studies is that because the acquisition of data by drug use is part of the reimbursement procedure to pharmacists, the validity of such data is strengthened greatly. There is no need to rely on physician recall or a second set of records kept by pharmacists to learn what drugs have been prescribed.

The various data banks available have been seriously underutilized in the past and have great potential value if used in innovative ways in the future. In theory, they are capable of following the drug-prescribing and drug-taking behaviour of patients, either by individual patients or by nationwide patterns of drug use.

2.3.2.1 Specific States

In **Oregon** Berkanovic (1974) researched the difficulties which were encountered in attempting to analyse costs and utilization data contained in Medicaid claims tapes. Three classes of problems were encountered: a) inaccuracy; b) missing data; and c) lack of standardized reporting conventions. Taken together, Berkanovic concluded that these problems seriously compromised the ability of the investigator to make a meaningful analysis of utilization experience which the data presumably recorded. Although this study is often quoted in a negative sense, it would appear that the quality of Medicaid records has improved greatly. The conclusion that the Medicaid record system in Oregon and in a number of other states "is an inadequate tool for research" appears to be no longer valid in the light of the numerous studies which follow.

Tennessee reimburses medical care providers for services rendered to persons who qualify for the four Medicaid programs: Old Aged Assistance; Aid to Blind; Aid to Families with Dependent Children; and Aid to the Disabled. Each patient's birth date, sex and race are recorded in master eligibility files. Outpatient claim payment files include patient and physician numbers, service date, procedure and diagnosis. The physician number is also recorded for drug prescriptions for ambulatory patients.

The prescribing of chloramphenicol in ambulatory practice involving Tennessee Medicaid recipients was described by Ray et al (1976). Diagnosis linkage was conducted as follows. Pharmacy claims for chloramphenicol were linked with the most recent of the prescribing physician's claims. Claims for physician services more than 60 days before filling the prescription were excluded. Claims with diagnoses compatible with infection were linked. Because physician claims for recipients of Old Age Assistance do not contain diagnosis, the pharmacy claims for these patients could not be linked. Also, those few prescription claims that failed to identify the physician could not be linked.

The same system was used to investigate prescribing of tetracycline to children less than eight years old in a two year epidemiological study (Ray et al, 1977). The use of tetracycline in children less than eight years of age is associated with a number of adverse effects including dental staining, enamel hypoplasia, inhibition of bone growth, "bulging fontanelle syndrome", candida albicans superinfection, gastroenteritis, phototoxicity and rashes among others. In January 1975 the Committee on Drugs of the American Academy of Paediatrics published a position paper entitled "Requiem for Tetracyclines" to publicise this important matter.

The study population consisted of ambulatory children less than eight years of age who received prescriptions through the Tennessee Medicaid program during the two year period from August 1973 through July 1975. Children were identified who were given prescriptions for tetracycline, doxycycline and methacycline in capsules, syrup or drops. The Medicaid files used were described in the previous report.

Pharmacists must specify the drug name, strength, number of units dispensed and costs to be reimbursed. The MMIS requires a recipient code as well as a physician code for every drug transaction. This makes it possible to develop profiles of particular patients or physicians (masked for confidentiality as required) for a variety of research and quality assurance purposes. Serious financial and legal disincentives exist to discourage inaccurate reporting of data.

The quality of care in the **New Mexico** Medicaid program between 1971 and 1975 was described by Lohr et al (1980). Data from the program have been used to assess the quality of antimicrobial prescribing.

Therapeutic drug use for the **Florida** Medicaid program has been reviewed by Groves (1985). In 1982 the Florida Department of Health and Rehabilitation services contracted with the Florida Pharmacy Association to administer a Medicaid DUR program for the state. The objective was to reduce the rate of morbidity associated with inappropriate drug therapy. The paper describes the Florida DUR program and summarized its first two years of operation. This program used the vast amount of data entered into MMIS by Electronic Data System Federal Corporation, the fiscal intermediary for the states. MMIS is capable of generating comprehensive medical history profiles that historically have been used only for the detection of Medicaid fraud and abuse. By limiting the use of MMIS data for this purpose rather than sharing the information with health care providers, states have often overlooked a valuable resource for improving the quality of health care for the Medicaid population.

In 1982 the State of Florida targeted the prescribed drug program, the largest category within the Medicaid program in terms of recipient use, as an area in which to implement health care cost containment measures. Review of exception profiles is conducted monthly by one of five regional DUR committees composed of four pharmacists and one physician. The DUR committees review profiles of patients in their geographic regions to identify profiles that warrant further examination based on: a) overuse or underuse of medications (patient compliance problems); b) contraindicated drug combinations or drug interactions; c) drug therapy contraindicated by diagnosis; and d) iatrogenic secondary complications seen after long term use, or adverse complications occurring within a short period of time.

The therapeutic criteria are developed and updated by a review committee consisting of physicians and pharmacists who represent the Colleges of Medicine and Pharmacy, University of Florida, the Florida Medical and Pharmaceutical Associations and Health and Rehabilitative Services. The committee identifies high risk drugs, drug use characteristics and disease states that represent the greatest potential for drug therapy problems among Florida Medicaid patients.

In the Florida Medicaid program, computer generated medical history profiles were used to identify patients at risk for drug induced illnesses. Health care providers can be notified of potential problems with patients' drug regimens and are asked for a response. Patient profiles are monitored for changes and follow-up letters are sent to the health care providers as warranted.

Psychotropic drug usage in an ambulatory elderly population in Dunedin, Florida is described by Stewart et al (1982). The Dunedin program began in July of 1975 to screen elderly participants on an annual basis for previously undetected medical disorders. Persons participating in the program are referred to private physicians for follow-up care when a medical disorder is detected.

Participants are scheduled for screening appointments by telephone or personal visit approximately five months prior to their visit. The week before the scheduled visit, a letter is mailed to remind the participant of the appointment and a detailed health questionnaire consisting of about 180 questions enclosed. A form is also included for listing current medications and the participant is asked to list all prescribed and nonprescribed medications used on a regular basis. For each medication the person is to indicate the therapeutic use (e.g. hypertension, nerves, laxative, etc.) and how frequently the product is used. To assess the duration of use the participant is asked to indicate whether the product has been used less than one month, one month to one year, one to two years, or longer than two years. On arrival for the appointment information on the questionnaire and drug history form is reviewed with each participant by a nurse.

Medications are coded using a modification of the therapeutic and pharmacologic classification of the World Health Organization. Psychotherapeutic agents were divided into hypnotics, sedatives, minor tranquilizers and antidepressants, and neuroleptics. Analyses are then conducted to determine the characteristics of use by age and sex. The same data base has been used to examine antacid use (Stewart et al, 1983).

The Inter-Society Committee on Antimicrobial Drug Usage conducted a survey of general hospitals in **Pennsylvania** (Kass, 1978). From 194 approved general hospitals in Pennsylvania, 20 were chosen at random so that the sampling of the hospitals on the basis of bed size (e.g. over 300, 150 to 300, and fewer than 150 beds) was considered. The Inter-Society Committee on Antimicrobial Drug Usage was formed by the American College of Physicians and consisted of representatives of that college, the American College of Surgeons, the American Academy of Paediatrics, the Infectious Diseases Society of America, the American Academy of General Practice, the Centre for Disease Control, and the Commission on Professional and Hospital Activities. Cooperating closely were the American Medical Association and the Bureau of Quality Assurance of the Department of Health Education and Welfare (HEW).

2.3.2.2 USA At Large

Drug usage review in long-term care facilities was conducted by Stewart et al (1976). The usage of ten drugs in five long-term facilities was reviewed to evaluate the effectiveness of a five-step systematic method of drug use review.

This five-step systematic approach to medical care review studies will maintain consistency and assure acceptability. The first step, selection of the health problem to be studied, should depend upon: a) the severity of the problem; b) its impact on the health care system; c) the potential for improving the system through studying the problem; and d) the potential use of the problem as a tracer.

The second step is development of criteria of care for the specific problem being studied. Process criteria are established so that immediate and long-term outcomes can be evaluated. This measured information is also used to assess the appropriateness of the initial process criteria.

Step three is measurement of specific medical care performance data and comparison with the criteria. This is an extremely critical step and its success depends upon proper selection of the problem and the development of appropriate criteria.

Step four is the establishment of an audit committee evaluation process. This will most likely be done by the facility's utilization review committee whose most difficult task will be to establish medical care standards of acceptable performance.

Step five is the design and implementation of educational activities. This activity has probably been the most neglected by DUR committees, but it is necessary since it completes the provider feedback loop and is designed to improve the level of care and reduce unnecessary expenses in the long-term care facility.

In each of the facilities data were collected on abstract sheets designed to indicate when a patient's drug usage did not conform with the criteria established by a committee of health professionals. Incidents of nonconformance were then examined. This systematic approach to identify drug usage patterns can be used by pharmacists to coordinate sample studies and to fulfill their consultant role in long-term facilities as required by federal regulations. The following definitions were approved by the National Professional Standards Review Council on November 26, 1973:

a) Norms: Medical appraisal norms are numerical or statistical measures of usual observed performance.

b) Criteria: Medical criteria are predetermined elements against which aspects of quality of medical care may be compared. They are developed by professionals relying on professional expertise and on the professional literature.

c) Standards: Standards are professionally developed expressions of the range of acceptable variation from a norm or criterion.

The use of medication in a residential institution for mentally retarded persons was reviewed by Silva (1979). The types and dosages of medications administered to a large group of institutionalized mentally retarded persons were summarized. The subjects of this investigation were residents of nine housing units at a large state institution for retarded persons. These units housed a total of 260 clients who were chosen from the remaining units for inclusion in the investigation because they were employing a modernized system of computerized drug dispensation, thus drug information on the residents of these units should have been highly accurate. The units studied were "open units" with the residents having the freedom to come and go for meals, work, school and other activities.

The medication data were obtained for each client in the sample from the institution's pharmacy records following authorization from the institution's Committee on Research. The investigation covered a span of three months. All drugs administered to clients in the sample during that period were reported.

Drug prescribing and use in an American community was presented by Stolley et al (1972). Since 1963 a computerized prescription recording system had been monitoring 85% of the prescriptions dispensed in a defined geographic area in the mid-Atlantic states, with hospital pharmacies being excluded from the study. The population studied comprised those patients who received a prescription from a doctor and presented it to a community pharmacy to be filled. If they presented it to the hospital pharmacy, an out-of-county pharmacy or did not fill it at all, the prescription recording system did not capture it.

The prescription recording system permitted the storage and retrieval of the following information:

a) Patient drug profiles for individual patients: this is a list of all prescriptions dispensed, by therapeutic categories and specific name that includes refills, quantity prescribed, dosage form, expenditures, and code name of prescribing physician;

b) Physician prescribing profile for individual physicians: this is a list of all prescriptions presented to the community pharmacies, by therapeutic category and specific name including refills, cost of the prescriptions issued, quantity and dosage form prescribed, number of different drugs prescribed, and the most frequently prescribed drugs; and

c) Community drug consumption profile for the community: this gives the total prescriptions issued, including refills, total expenditure for drugs, and selective characteristics of persons receiving the greatest number of drugs.

Drug use in the United States in 1981 is reviewed by Baum and Kennedy (1984). Outpatient prescription drug use was based on pharmaceutical marketing data. Data were derived from the subscription data base purchased by the FDA from two pharmaceutical marketing services. Alpha System was purchased from Pharmaceutical Data Services (PDS) of Phoenix, and National Prescription Audit (NPA) from IMS America, Limited, Ambler PA. Both measure the "retail outflow" of prescriptions or the rate at which drugs move out of the retail pharmacy into the hands of the consumer via a formal prescription. The systems are based on new and refill data from computerized pharmacies.

These authors comment on the characteristics of the information used to provide information about drug use. They indicate that estimates of drug use can vary greatly if different points in the drug distribution chain are measured. The total amount of a drug produced by a manufacturer is generally much larger than the amounts being shipped to retail pharmacies. Even in more closely related points in the distribution process, quantities need not be identical. For example, the number of prescriptions written by physicians for specific products and the number dispensed by pharmacists may differ because of generic substitution and patient noncompliance. The data on the number of prescriptions containing specific drug chemicals presented in this article provide a better estimate of actual population exposure, but are limited in that they do not consider prescription size.

2.3.2.3 Veterans' Administration (VA)

In 1975 the VA directed the implementation of DUR programs as part of their systematic internal review process (Krischer et al, 1982). In 1980 the VA system attempted to investigate the extent of the DUR programs, their costs and their effectiveness. To do so, all 172 facilities in the VA system were surveyed. The resources for DUR are reviewed. Application of the VA drug utilization service included the survey of prophylactic antibiotic prescribing habits among chiefs of surgical services of the VA administration (Munster et al, 1979).

2.3.2.4 Computerized on-line Medicaid pharmaceutical analysis and surveillance system (COMPASS)

The computerized on-line Medicaid pharmaceutical analysis and surveillance system, a new resource for post marketing drug surveillance, is described in detail by Strom et al (1985). COMPASS is a very large computerized data base of Medicaid billing data. It is designed to permit a researcher to enrol and analyse cohorts of patients exposed to a drug or patients with specific diseases and to compare them with matched or unmatched control groups. COMPASS derives its data as a byproduct of the Medicaid Management Information System (MMIS).

COMPASS was originally conceived by Health Information Design Inc. (HID) and has been under development by HID since 1979. Initially, HID undertook on-site evaluation of the MMIS system of six states and chose the data from Michigan and Minnesota (with an initial Medicaid population of 1.2 million, now increased to 2.0 million). More recently, Medicaid data from Florida, Missouri, Nebraska, Arkansas, Mississippi, Ohio and Virginia have been added. HID provides these states with an MMIS based drug utilization review program and, as part of this program, has obtained the right to use the MMIS data it receives for post marketing surveillance (PMS). With these additions the total COMPASS population is now over five million patients.

COMPASS software is currently installed on a mini-computer manufactured by Wang Laboratories. Drug and diagnosis data processed by each state's MMIS is extracted and forwarded to the HID offices. Patient and provider identities are kept strictly confidential. The extract tape is sorted by patient identification number, service type/code and date of service, then edited for incomplete or erroneous data elements. During the edit stage, specifically developed binary codes are assigned to each National Drug Code (NDC) and each International Classification of Diseases (ICD-9-CM) code. This maximizes the on-line storage capacity of the patient history files.

Information on drugs and diagnosis can be accessed by a variety of coding methods. For drug information, data can be accessed with NDC codes, generic codes, specific therapeutic class codes, or user defined code groups. Similarly, it is possible to access diagnosis information with ICD-9-CM codes, disease category class codes or user-defined code groupings. Primary medical records cannot be obtained from physicians, hospitals and other sources unless the number of requests is relatively limited.

2.3.2.5 Independent Health Insurance Systems

The health status, sociodemographic factors, and the use of prescribed psychotropic drugs in the Rand Health Insurance Experiment (HIE) in California are discussed by Wells et al (1985). The relations between sociodemographic factors, health status and use of prescribed sleeping pills and tranquilizers were examined from self-reported questionnaires collected at enrolment. The Rand Health Insurance Experiment had a random sample of the nonaged, noninstitutionalized, civilian population in six U.S. sites.

Between 1974 and 1976, the HIE enrolled families in six sites: Dayton, Ohio; Seattle, Washington; Fitchburg and Franklin County, Massachusetts; and Charleston and Georgetown county, South Carolina. Participating families were randomly assigned to one of fourteen different health insurance plans that had different levels of costs sharing, using the Finite Selection Model (Morris, 1979). Families were enrolled in the insurance plan as a unit with only eligible members participating. No choice of plan was offered; the family could either accept the experimental plan or choose not to participate.

The sample for the study included all individuals 18 years of age and older who were enrolled and who completed a self-administered enrollment questionnaire (2% of enrolled adults). The enrollment questionnaire included the Sleeping Pills and Tranquilizers Battery, which elicits information on whether sleeping pills and/or tranquilizers were prescribed during the previous three months, and the frequency at which they were used during this period. The Mental Health Inventory (MHI), a 38-item instrument designed specifically to measure mental health in the HIE, was also applied along with a number of other scales of health status. The social contacts scale was constructed from three items that measured the frequency of contacts with friends and relatives in the previous year.

To examine the relations among drug use, sociodemographic factors and health status, four multiple regression equations were used: one each for the probability of sleeping pill and tranquilizer use; and one each for the frequency of sleeping pill and tranquilizer use, given any use. The authors tested interactions between sex and mental health and between physical and mental health and the probability of prescribed tranquilizer use.

Drug utilization review in a health maintenance organization (HMO) including aspects of methodology is described by West et al (1977). West and her colleagues describe an experimental drug utilization review program which was developed for a HMO. The objectives of the program were to develop and implement an ongoing mechanism for reviewing drug use using criteria based on the scientific literature, and to evaluate the effect of the DUR program on physicians' prescribing patterns. Seven therapeutic categories of drugs, accounting for over 65% of prescribing, were selected and criteria were developed for their use. The DUR procedure is described briefly.

The drug utilization and expenditures of a medically indigent population at the Kaiser-Permanente Medical Care Program was examined by Johnson et al (1978). The objectives of this report were: a) to provide baseline data about drug utilization within a medically indigent population receiving totally prepaid prescription benefits in a prepaid groups practice comprehensive medical care system; and b) to identify any changes occurring in drug utilization over a period of years and to identify factors associated with any changes observed.

The setting is the Kaiser-Permanente Medical care program, a group practice medical care system that provides prepaid, comprehensive service to a defined population, which includes a medically indigent group for whom all medical services are totally prepaid by a HEW-funded Neighbourhood Health Centre program. The group receives all prescription-legend drugs, over-the-counter drugs, and various medical supplies at no expense when prescribed by a Kaiser-Permanente physician.

The prescriptions received by the study population from pharmacies operated by the medical care program have been continuously collected, coded, edited and maintained on computer tape. These data are the basis for the analysis.

2.3.3 United Kingdom

Since 1961 the British Ministry of Health has revised the basis on which information is obtained for the kinds of drugs, dressings and appliances dispensed under the National Health Service Pharmaceutical Services by pharmacist contractors and appliance contractors.

Information on drug classification includes the identity of the drug, whether it is non-proprietary or proprietary, the therapeutic class of the drug, and the physical form of the medication. For proprietary drugs, the year of introduction, the manufacturer and the classification of the drug in therapeutic terms is recorded. Annual summaries of the analyses are presented in the Annual Reports of the Ministry of Health for England and Wales and by the Home and Health Department in Scotland.

Information about the actual overall total numbers and costs of prescriptions dispensed in different areas can be obtained during the pricing process for one month in each year for each executive council area. The total number and costs of prescriptions ordered by each doctor are obtained as part of the general procedure for investigating the prescribing costs of all general practitioners.

The Prescription Pricing Authority (PPA) is responsible for the payment of the pharmacist. The information for a particular region is forwarded to the Family Practitioner Committee (FPC) for that region. The total number of prescription forms, total number of prescriptions, the average number of prescriptions per form, the basic and total costs and the average cost per prescription are calculated. From knowledge of the total number of persons on each physician's NHS list the average number of prescriptions per person and the average total cost per person can be defined. If a given practice uses 1.25 times or more the average for that area, the Investigation Division of the PPA is asked to take statements. Furthermore, the PPA can screen all drugs from a given practice or group. Other roles of the PPA include the identification of inappropriate prescriptions for substances which are defined as cosmetics or foods except under unusual medical circumstances. In the U.K. physicians who are found to be responsible for inappropriate prescribing of these substances can have the costs deducted from their salaries.

The PPA interacts with the Committee of Safety of Medicines to provide information on overall drug utilization. Furthermore, it has been possible to identify the patients who have received particular drugs and to screen them for possible adverse effects.

Binns (1980) makes the comment that the PPA uses the well established technique of management by exception and concentrates on departures from the norm. This is useful especially when you are dealing with what is obviously wrong but it does not follow that the norm is necessarily right. At present it is difficult to know what is right because the huge differences between countries in the number of drugs available and in their usage have no evident effects on national mortality and morbidity statistics.

Binns argues that we must try to develop better methods of assessing whether the economic and clinical effects offset the cost or justify the risk. Only when the therapeutic auditor can see both sides of the balance sheet would a true and fair view of the whole accounts situation be seen.

McDevitt (1979) has indicated that the confidentiality of data has made it increasingly difficult to get the information necessary for conducting adequate DUR. Furthermore, the information does not include OTC drugs nor does it review the prescriptions for private patients who are responsible for their drugs prescribed outside the National Health Service (NHS). The system is not linked to a disease state and the appropriateness of therapy cannot be adjudicated.

Wade (1984a) reviews the background of DUR and attributes the credit for the concepts to Sir Austin Bradford Hill who was the leading exponent of the discipline of the "randomized clinical trial" and later to the epidemiologist Dr. Archibald Cochrane. Wade states that Cochrane's work and teaching had a great deal to do with the first study of drug use in Northern Ireland in 1962-63 which was, as Wade describes it, "a study of the epidemiology of the prescribing of drugs".

In Northern Ireland each pharmacy sends all the NHS prescriptions to a central bureau (the local office of the PPA) for pricing and repayment at the end of each month. The three month total for each area represents the amount of drug actually supplied on prescription to patients outside hospitals. Data on drugs supplied to hospitals are collected separately for the province as a whole and represents approximately 8% of the total quantities prescribed. Information on the prescribing patterns of Northern Irish physicians are shared on a confidential basis with the Department of Therapeutics of the Queen's University of Belfast.

The study of amphetamines in general practice by Hood and Wade (1968) of the Queen's University of Belfast is one of the earliest drug utilization studies ever conducted. Wade and Hood investigated all prescriptions for amphetamines issued by general practitioners between April and June 1966. Psychotropic drug prescribing, derived from the computerized pricing data in Northern Ireland from 1966 to 1980 is described by King et al (1982). These same data are discussed in a further review by King and Griffith (1984) and are of interest in monitoring the possible influence of civil unrest on mental health and drug utilization.

A description and assessment of usefulness of the Hereford Hospital Prescribing Study is described by Barnett et al (1981). The mode of operation of a computer based operation system, designed to link information by drug usage to diagnostic data, is described. Data capture of hospital activity analysis information is collected by standard procedures applicable to all patients. The diagnosis and operations are entered after the patients' discharge. Information about the drugs is abstracted from the patients' hospital medical records onto separate forms.

The data are punched and then processed by the computer, an ICL 1904. If errors are not found after a check by the validating program, the information from the two forms is merged to produce the patient record and the master systems file of drug information. This file exists physically on tape, one tape for each year of the systems operation. Recently the systems file has been converted into fixed length records, and is now called a fast access file. This has been done to ease analysis of the data. Each record now consists of some patient identification information and data about one drug. If a patient had three drugs then he will have three records, each of the same format. Aspects of the system are described in detail.

The studies performed have included an investigation of whether or not prescribed drugs are being administered properly, the administration of unprescribed drugs, changes in drug usage, prescribing costs, comparison of drug efficacy by duration of hospital stay, and investigation of adverse drug reactions (e.g. GI bleeding associated with arthritis medications). The authors indicate that the system has had a considerable impact on all matters connected with drug usage in the hospital, though the improvement in care and the more efficient administration of drugs cannot be estimated in cash terms.

The usage of antimicrobial agents was studied in 18,163 patients in the National Prevalence Survey in 1980 (Leigh, 1982). This national survey examined a sample of approximately 10% of the total of acute beds in England and 43 hospitals were involved in the study. 4037 (22%) of patients were receiving antimicrobials. The hospital notes for all patients were examined for the use of antimicrobial agents, and details of the particular compounds and route of administrationn were entered on the survey questionnaire. No details of dosage or length of treatment were recorded. The antimicrobial agents were grouped in 14 categories.

Drug usage and adverse drug reactions in pediatric patients in Scotland are discussed by Whyte and Greenan (1977). The development of epidemiological methods for the study of adverse drug reactions has been reviewed in connection with the presentation of data obtained by intensive monitoring of 1000 admissions to a medical pediatric unit.

Successive admissions to a medical paediatric unit (48 beds) with regional responsibilities for cardiac investigation and the treatment of leukemia were intensively monitored using a method similar to that of Slone and his co-workers (1966). 1000 admission episodes, involving 909 children, occurred over a ten month period, but 68 were excluded from the study when the children required a general anesthetic or were transferred to another ward. A record of each child's age, sex, weight, height, diagnosis and duration of stay in hospital was completed in addition to information on pre-admission therapy and previous adverse drug reactions which was obtained by interview with the parents.

The use of duplicate prescriptions as an aid to research and review is presented by Hamley et al (1980). A method of studying patterns of prescribing and related morbidity in general practice is described. Describing data were automatically duplicated onto a no carbon required (NCR) prescription pad. Additional information about diagnosis and indication for each drug, and indication of whether the drug was newly prescribed or a repeat, and a patient identification code were entered onto the bottom copy.

The method is thought to offer an efficient means of collecting data which can be applied to individuals or groups of doctors to improve patient care and health and achieve rational prescribing. In this system drugs were coded centrally using the Department of

Health and Social Services (DHSS) Drug Master Index. Clinical indications were coded using the International Classification of Health Problems of Primary Care (Royal College of General Practitioners, 1976). These investigators identified the major therapeutic classes of drugs. The form can be modified to identify consultations in which no drug was prescribed. The information was fed back to the physicians and subsequent studies have been able to monitor changes in pattern of prescribing.

The total prescribing in an urban general practice was recorded over a six month period and classified according to the length of time that the drugs were continued (Murdoch, 1980). All prescriptions written in the Medical School Teaching Practice in Dundee, Scotland between October 1977 and March 1978 were duplicated. The following information from each prescription was coded and stored on computer files: a) identity, age and sex of patient; b) drugs prescribed (group and individual coding by the Department of Health and Social Security Coding); c) daily dose of drug; d) days supply prescribed; and e) indication for each drug prescribed (coded using the International Classification of Health Problems for Primary Care (WONCA 1976).

The drugs prescribed for children in a Tayside hospital in 1974-75 were surveyed using the computer files of over 4,000 children each year (Moreland et al, 1978). Antimicrobial drugs accounted for approximately one third of the total drugs used in children and one half of all patients received at least one drug from this class.

Drug monitoring in general practice in the United Kingdom is presented by Skegg (1982). Skegg was authorized to obtain the prescriptions from the pricing bureau. He indicated that this required long and frustrating negotiations in which he was shunted from official to official. Nevertheless his work with Sir Richard Doll was responsible for several important clinical associations with drug use. He concludes that record linkage would be a valuable method of monitoring drugs prescribed in general practice. It would reveal unsuspected hazards of drugs as well as provide more information about adverse effects discovered elsewhere. A full scale project would be particularly valuable for detecting delayed effects, such as the induction of cancer, sudden death outside hospitals, and effects on the fetus; all of which are difficult to study by other means. Apart from revealing the hazards of some medicines, a record linkage scheme would provide positive evidence for the safety of many others. Furthermore, it might lead to the discovery of unexpected benefits of drugs.

The results of Skegg's work are described in further detail by Skegg et al (1977). The population studied consisted of people registered with 19 general practitioners. Basic information about the people in the population (e.g. sex and date of birth) was available from the computer records of the Oxford Community Health Project. The PPA provided photocopies of all FT 10 prescription forms bearing the stamps of the participating doctors. These included prescriptions written by the practitioners' assistants and locums who used the prescription forms of the principals, but not those written by other medical practitioners (e.g. hospital doctors). The methods ensure that only prescriptions actually dispensed are included.

Information from each prescription was coded and added to the patient's computer record. All complete items prescribed were treated independently, irrespective of whether two or more were written n the same form. In this report a "prescription" therefore means a prescription for one medicine. Prescriptions for items other than drugs were omitted. The practitioners were not provided with information about their prescribing until after the period covered by this report, so their prescriptions were not biased.

Skegg (1984) summarizes his work in the paper "Relation between drug utilization and morbidity, a record linkage study". He concludes that the opportunities for this type of research are greatest in countries with highly organized health services, such as the Scandinavian countries and the United Kingdom. Linkage with morbid events was concluded through a separate computer file which contained data from the group practices in which general practitioners were recording their diagnosis in an "E" book. This file was analyzed to reveal associations between drugs and events.

2.3.4 The Nordic Countries

2.3.4.1 Sweden

Drug utilization in Sweden is described by Bergman and Sjoquist (1984). The available sources of information on drug utilization in the Swedish population at large are reviewed. They comprise wholesale statistics, drug deliveries to hospitals and prescription data. Drug consumption is expressed in DDDs per capita, where DDD is the average recommended dose for the major indication of the drug. Under ideal circumstances (i.e. drugs used continuously on one indication) the number of DDDs per population ought to agree with morbidity data. This turns out to be the case with anti-diabetic drugs.

The pitfalls of this unit of measurement include major discrepancies between recommended and prescribed doses, and the use of the drug on vastly different indications such as neurosis and psychosis in the case of neuroleptics. Nevertheless the DDD methodology may serve as a therapeutic audit in attempts to follow and influence therapeutic habits of health in personnel in hospitals and primary health care.

Wholesale data combined with individual base prescription data are particularly useful in this regard. Drug use in individual patients is available through the continuous recording of purchases of prescription drugs in a sample of 17,000 inhabitants of the county of Jamtland (Boethius, 1977) and 21,000 inhabitants in the

Tierp area (Riezenstein et al, 1979).

Since 1965 the total sales of drugs to pharmacies and hospitals have been recorded by Svensk Lakemedelsstatistik AB (Swedish Pharmaceutical Data Limited -LSAB). The sales statistics are published quarterly in the Swedish Drug Market and are distributed to prescribers in the pharmaceutical industry, to the National Board of Health and Welfare (Department of Drugs), and to the National Corporation of Swedish Pharmacies. The latter organization has produced such statistics since 1975 for the country as a whole, and for each county or even smaller geographic areas as desired. The invoices for drugs delivered to pharmacies by wholesalers are the basis of these statistics. Based on hospital invoices, statistics on the total sales of drugs to hospitals have been published since 1974.

A continuous nationwide prescription survey has run since 1974. A sample of 1 in 288 of all prescriptions filled in Sweden in a year has the following data recorded: age and sex of the patient; the name and amount of drug prescribed; daily dose; patient fee; and total cost (Kristoferson and Wessling, 1977 and Wessling, 1986).

A Diagnosis and Therapy Survey has been running in Sweden since 1978 as a collaborative project between LSAB, the National Corporation of Swedish Pharmacies, the Swedish Medical Association and the National Board of Health and Welfare. A running random sample of physicians (about 1750 doctors a year) have been asked to participate. During the study week all prescriptions are recorded on self-copying prescription forms, where the indication for each drug is added (Agenas et al, 1980). The diagnosis or symptoms are coded according to the International Classification of Diseases (ICD 1965).

The difficulties of obtaining an accurate estimate of the overall utilization of a common drug like diazepam are obvious. For example, in 1981 four companies furnished the Swedish drug market with about 70 products containing diazepam: oral, rectal, and parenteral dosage forms in various strengths and pack sizes and different prices. It is even more complicated to compare the utilization of diazepam with closely related drugs such as chlordiazepoxide, oxazepam and nitrazepam. To overcome these difficulties a so-called defined daily dose (DDD) was established for each drug after consulting experts in various fields in pharmacotherapy.

The Nordic countries have agreed to use the Anatomical-Therapeutic-Chemical (ATC) Classification system which is a five level code and a further development of the three level EPhMRA/IPMRG code. At its fifth level the ATC code identifies single chemical substances. As an example all diazepam preparations have the code N 05 BA 01.

Since the mid 1970s the National Corporation of Swedish Pharmacies has annually published statistics on drug utilization (Svensk Lakemedelsstatistik, 1981) containing sales data expressed in DDDs. The Nordic countries have agreed to use the DDD system as adopted and recommended by the WHO Drug Utilization Research Group (WHO, 1979). The validity of wholesale data has been tested by comparing wholesale and prescription data, which were found to agree fairly well provided the observation period was sufficiently long and the patient base large enough (Bergman, 1978).

The reliability of wholesale data also has been investigated by Bergman (1978). Swedish wholesale figures for a quarter of a year were used for the comparison of antidiabetic drugs, based on "daily doses" per thousand inhabitants. Antidiabetic drugs distributed on a wholesale basis in the island of Gotland were compared with those distributed on a prescription basis. Additional information was gathered by interviews, questionnaires, and hospital records etc. from a sample of patients (n=54) and their prescribing doctors (n=37).

Gotland, Sweden is a well defined rural area with a 1972 population of 53,805. Total monthly sales statistics of insulin and oral antidiabetics for the island were made available by the LSAB. Simultaneously, prescriptions of such drugs to patients (n=868) and supply figures of hospitals (n=3) from the central pharmacy in Gotland were collected. Total sales statistics and prescription figures were compared on the basis of daily doses per one thousand inhabitants.

A number of actual studies is described in this and other papers. National and international comparisons of anti-diabetic drugs and psychotropic drugs are presented elsewhere. The paper further discusses the role of the DDD methodology. The author points out that there are problems with drugs used in markedly different doses on different indications and for drugs used in short term treatment (e.g. antibiotics and minor analgesics). Furthermore, the DDD methodology does not take into account differences in the frequency of combination therapy.

A further source of information on drug usage in Sweden at large is a nationwide interview survey of a random sample of the population aged 16 to 74 years (Survey of Living Conditions in Sweden, National Central Bureau of Statistics). According to this survey 25% of DDDs fell outside (mainly above) this age span. Even higher figures were found for cardiac glycosides (45%), diuretics (36%), and oral diabetic drugs (33%). This has important clinical pharmacological implications since drug elimination, particularly drug excretion, is slowed down in the elderly. Moreover, the Jamtland county study, where individual dosage schedules may be studied in different age groups, has revealed that many elderly patients do not get proper adjustment of the doses of drugs such as digoxin, sulphonamides and tetracyclines which are dependent on kidney function for their excretion. International data on drug utilization in the elderly also reveal that much more attention should be given to the concept of geriatric dosing regimens for such drugs.

In hospitals continuous monitoring of drug utilization expressed in DDD/bed-day may serve as an inexpensive and simple basis for discussion of pharmacotherapeutic routines and in the planning of continued drug education of health personnel. Similar methods are badly needed in primary health care, where approximately 70% of all drugs are delivered.

Drug delivery statistics in Sweden are converted to DDD by computerized routines. The statistics are available through the National Corporation of Pharmacies to many doctors and pharmacists and local Pharmacy and Therapeutic Committees, which so far function mainly in hospitals. Such information should be valuable in planning and evaluating drug information programs, and in identifying drug problems requiring further investigation.

The sources of information available in Sweden give a rough estimate of drug utilization. The medical relevance of the data obtained must be thoroughly evaluated and when problem areas are detected more elaborate studies often have to be conducted to get the detailed information necessary for clinical judgment of therapeutic quality.

The authors conclude that drug utilization research now has to focus on the linkage between recordings of prescriptions and relevant clinical data on effects and side effects of drugs. Technical facilities are already available for studies, but the quality of the clinical pharmacological data leaves a lot to be desired. The development of this research also will depend on policies concerning the relative importance of the individual patient confidentiality on the one hand, and drug safety and drug efficacy in the population at large on the other.

The process of auditing hospital drug utilization is described by Bergman et al (1980). The method involved the study of DDD units of the drugs under evaluation for each ward and the total was divided by the number of bed days. The authors conclude that this is a relatively inexpensive indicator of drug utilization in the hospital and is a suitable basis for therapeutic audit.

The pattern of drug usage as obtained from the continuous recording of prescriptions in the county of Jamtland, Sweden is described by Boethius (1977). Since 1970 about 16,600 persons have been monitored. This corresponds to all individuals born in the same four days in each month. Data from prescriptions filled at the pharmacies are continually compiled in drug lists. These contain the patient's identity number, denoting for example age and sex, the year and week the drug was purchased, the prescribing doctor, the total amount and dosage of the drug, and the type of prescription record. The indication for the prescription is not available. Drugs obtained without prescriptions are not recorded.

Relationships between drug utilization and morbidity patterns are presented by Westerholm et al (1984). The question raised by Westerholm and her colleagues in this review paper is: Do drug utilization data, versus other health care data - such as causes of death and sick reports, discharge diagnosis and number of days on the sick list - give a similar picture of the health status in Sweden?

The data reported by Bergman and Sjoquist (1984) have been analyzed to look at the association in prescribing and diagnostic categories from various national sources in Sweden. The most common causes behind sick reports, the Diagnosis and Therapy Survey of October 1980 through September 1981, the sales to hospitals of drugs in 1981, the most common diagnosis at discharge of inpatients in 1977, and the most common causes of death in 1977 have been utilized on a region by region basis to enable the authors to make comparisons between the sales of particular drugs and the reports from diagnostic sources of actual disease states.

They conclude that although a number of discrepancies exist between these sources of information, analyses show that the similarities between the pictures they give of health status are considerable, provided due consideration is given to the fact that, for self-evident reasons, certain illnesses and injuries are not to be found in all the sources.

Meirik et al (1979) describe an interesting study of contraceptive and intrauterine device use to examine fertility rates in a population. It is an example of how drug utilization data can be used to assess health and disease in a community. Applying the method to calculate the total fertility and abortion rates and use of oral contraceptives and intrauterine devices in Sweden in 1975, the authors noted 1.8 deliveries and 0.6 legal abortions per woman in 7 years use of oral contraceptives and 6 years use of intrauterine devices.

The nature of analgesics prescribed in Jamtland as a whole were reviewed by Gustafsson and Boethius (1982). Sources of data were described earlier.

The use of anti-Parkinson drugs in Norway, Sweden, Denmark and Finland between 1975 and 1979 is reviewed by Aquilonius et al (1981). This study reviews the use of anti-Parkinson drugs in hospital and in the community based on the total quantities of the drug sold in Norway, Sweden and Denmark, and on the amount sold in drug stores in Finland. The DDD per day per thousand patients is the unit of utilization. The utilization of anticholinergic medications in conjunction with levodopa can also be measured.

2.3.4.2 Norway

In Norway there is a single centralized wholesale system for medications. Drugs for chronic or prolonged illness are obtained free of charge.

Based on regional drug sales statistics, two counties with a consumption of hypertensives below average and two counties with above average consumption were selected for a prescription study among general practitioners (Baksaas et al, 1970). The first part of the study involved collection of all the GPs' prescriptions for antihypertensive treatment during the month of October 1975. Immediately afterwards the GPs filled in a questionnaire in which they described their diagnostic and therapeutic criteria and procedures for arterial hypertension. Both parts of the studies were analyzed and compared. Patient compliance and adverse drug reactions were also registered.

A two sheet prescription form was used during the investigation. Sheet one was the standard prescription form and sheet two was a duplicate with additional questions. The prescription copy included additional questions about patient identity, date of birth, initials, sex, and address. The type of consultation, whether at the doctors office or by telephone, was noted. The blood pressure (BP) and date before treatment, BP and date at last examination, and present BP and date were recorded. Coexistent disorders such as angina pectoris, arrhythmia and heart failure were also noted. It was additionally noted if this was a first time prescription, a re-prescription, an altered prescription (e.g. in terms of dose or prescription), or a supplementary prescription. Other regular medications were noted in terms of names, strength and dose of the preparation. Any side effects noted were also recorded. Other medical services as well as the physician's assessment of the therapeutic effect as good, medium, bad or none were also noted. The information on the prescriptions was transferred to digital codes to permit computer processing. Cooperating agencies were the Norwegian Ministry of Social Welfare, the Norwegian Health Directorate, the Norwegian Drug Monopoly, the Norwegian Medical Association, and the Norwegian Pharmaceuticals Society.

2.3.4.3 Denmark

A method for sampling reimbursed prescriptions in Denmark is described by Andreasen et al (1979). This paper presents a low cost method to obtain quantitative expression for the utilization, disposition and cost of drugs in Aarhus county, which has 500,000 inhabitants. The method is based on systematic utilization of all the information available on each prescription. Concepts of "entry parameters", "calculated units" and "derived units" are discussed. The units concern frequency of prescription and patient age and sex in relation to specific dose frequencies (weighted units or defined daily doses - DDDs). The possibility of creating a base for calculation of the frequency of certain diseases and of side effects of drugs is mentioned, and examples of the application of the method to certain categories of patients and to certain drugs are given. Some limitations of the method are included and it should be considered as a supplement to other more complete methods for the study of drug consumption.

For reimbursed drugs the following information may be obtained: a) a ten digit subject identification number from which age and sex can be derived; b) an identification number for the pharmacy; c) the date of sale of the drug product; d) the drug product identification number; e) the total dose prescribed; f) the daily dose prescribed or maximum daily dose; and g) the total cost of the prescribed amount.

These authors have developed a statistical table. Sampling was done with the aid of a computer using 1412 uniformly distributed random numbers. The possibilities and limitations of the system are discussed.

If the purpose of the study is to make statistically balanced comparisons between different population groups or between different time periods, it is necessary to specify the magnitude of change it is wished to show and the required confidence level. These requirements will influence and set necessary sample size. The value of the information obtained from an extended sample must always be related to the cost and collection of the information. For more specific purposes such as creating the basis for calculations of frequency of side effects, for example, or for relating prescribed daily dose to the age of the patient, large samples may be needed. The cost may be reduced by "selected sampling", i.e. only information from the relevant prescription blanks in the sample is coded and the others are just counted.

As the ultimate goal is still to obtain knowledge about the actual amount of active compound ingested by individuals, the method described here has both unpredictable (e.g. drug compliance) and predictable shortcomings. It is only possible to get information about drugs that are paid for by the public health service. Furthermore, no knowledge is obtained about drugs consumed within hospitals or used in the doctor's office. The method should be considered as an alternative and a supplement to others which also have their shortcomings (e.g. interviews, production sales statistics, and so forth).

2.3.4.4 Finland

Problems in the measurement of psychotropic drug consumption in Finland and Norway are reviewed by Hemminki (1982), who raises the issue of a significant problem with the define drug dose (DDD). Hemminki expresses concern about the value of DDDs in the study of psychotropic drugs since these drugs are used in widely varying doses depending on individual psychiatric indications.

She introduces the concept of 'defined exposure dose' (DED), a measure which estimates the potential chemical exposure of the population to drugs. A group of experts were asked to estimate the quantities of certain drugs that they thought would produce effects equal to diazepam 10 mg per day. The DED for several drugs was considerably different from the DDD. For example haloperidol with a DDD of 8 mg had a DED of only 1 mg. On the other hand the DDD and DED of phenobarbital were virtually identical at 100 and 108 mg respectively. Applying this technique, the comparable drug use in Norway and Finland was reviewed.

Hemminki also points out other problems in measuring psychotropic drug consumption which include the comparability of drug sales, physician prescribing and drug use. Some countries have a profusion of active substances, trade name products and combination drugs making calculations extremely difficult. Drug sales data are often secret.

Nationwide interview studies have shown that the use of non-prescribed vitamin supplements in Finland increased during the late 1970s (Klaukka et al, 1985). The data were derived from three nation-wide health interview surveys in Finland conducted in 1968, 1976 and 1978-80. The samples were representative of the entire non-institutionalized population. The Mini-Finland Health Survey was a major source of data of health status and health behaviour in Finns who were 30 years of age or older. The prevalence and number of persons in Finland receiving cardiac glycosides were estimated in connection with the general health survey (Impivaara, 1985). A population sample of 8000, representative of the adult Finish population, was studied.

The survey consisted of two main parts: health interview and health examination. The health interviews were carried out by local public health nurses who visited the examinees about 2 weeks prior to the health examination. Questions about the current use of drugs were included in the interview. The reported drugs were checked from the prescriptions or from the package labels. 7703 persons (96.3% of the sample) participated in the health interview.

The health examination was carried out by a mobile clinic unit of the Department of Social Insurance Institution. 7217 persons (92.2% of the sample) participated. With the invitation to attend the examination, the examinees received a questionnaire including questions about current medications. They were asked to bring along the prescriptions for the drugs they had taken during the preceding

12 months. No prior information about the digitalis study was given. Specially trained nurses checked the questionnaires and prescriptions, and recorded all drugs used by the patients during the previous 3 months. It was also recorded whether they took these drugs regularly or temporarily and had taken them during the preceding 7 and 2 day periods.

A postal inquiry including a questionnaire on drug use was sent to those who did not attend the health examination. A random subsample (20%) of participants in the health examination was reexamined about 3 months later. The repeatability of the questionnaire and the variation in reported use of drugs were estimated in this sub-sample. The long-term variation was estimated in a separate representative sample of 30-69 year olds drawn from the population register.

2.3.4.5 Iceland

In Iceland continuous data registration and analyses are not practical (Grimsson and Olafsson, 1977). Instead two *ad hoc* studies were carried out covering all prescriptions in Reykjavik: one in November 1972 and the other in November 1974. The following data were collected on the prescription form: a) the patient's name and number; b) doctor's code; c) name of drug, strength and dose form; d) quantity; and e) price.

The Icelandic National Register was computerized in 1952 and is updated yearly. Two identification numbers are used. The main one gives the date of birth in nine digits: the first six stand for date of birth (day, month, year), the next two digits are a serial number, and the last digit is a check digit. The other identification number, which is used widely by various institutions, is a number of eight digits which is issued at the age of 12 and indicates the person's name in alphabetical order. The main objectives of the study were: a) to collect information on doctors' prescribing habits and the drug use or abuse by the recipient; b) to provide a tool for the health authorities so that drug prescriptions could be controlled and the use of drugs monitored; and c) to provide statistics on drug-taking for the use of pharmacologists, sociologists, psychiatrists and psychologists etc. studying drug addiction. Systems for each of these elements are described.

2.3.5 Europe (apart from the U.K. and the Nordic Countries)

2.3.5.1. Federal Republic of Germany

Although Gross (1981) makes many comparisons of drug utilization in Germany with other countries, the sources of his data are not described. They appear to be mainly sales data. He recommends that the Pharmaceutical Manufacturers Association of the Federal Republic of Germany should follow the example of the British pharmaceutical industry in establishing a Medical Research Unit which has as one of its objectives "reviewing population health statistics in relation to the use of medicine".

2.3.5.2 Italy

Systems are not well described (Grassi, 1979). Data appear to have been developed from marketing reviews, from samples dealing with hospitals, practitioners, pharmacists, and "dealers of pharmaceutical products" and "elaborated by statistical methods".

2.3.5.3 Netherlands

The hypothesis that prescribing rationality is related to physician rather than patient characteristics was investigated by Haayer (1982). Haayer also examined the relationship between prescribing rationality and the use of different sources of drug information and agents by general practitioners. Prescribing rationality was assessed by a panel of experts with the case-history method. Data on the use of different sources of information were collected in a follow-up interview.

Prescribing of general practitioners was studied since they account for three quarters of all ambulatory prescriptions in the Netherlands. When the study began in 1979, there were 148 non-dispensing general practitioners in Twente; 17 were not considered for the study because of technical and methodological reasons.

Data were gathered by a written self-administered questionnaire, followed by a face-to-face interview. In the questionnaire data were gathered concerning rational prescribing and the age of the GP. The following four criteria were used to define rational prescribing: a) appropriate for the symptoms/disease presented by the patients and for which no better therapy exists; b) effective for the treatment of the symptoms/disease presented; c) safe, with as few side effects as possible; and d) the right dose and duration for the indication.

Using these criteria prescribing rationality must be judged in the context of indications. No such data (i.e. prescriptions with their associated indications) are available in the Netherlands, so this information had to be obtained directly from physicians. Two GPs and a clinical pharmacologist designed eight common practice case histories in which different possible treatment regimes could be followed. The GPs were asked what they would prescribe in these cases and to write a complete prescription.

2.3.5.4 Spain

Drug utilization studies as a tool for determining the effectiveness of drug use was examined by Laporte et al (1983). The data source was a collection system for drug utilization studies based on the sales figures of more than 20 pharmacies and the most important wholesaler in Spain. Data obtained with this system are periodically validated through comparison with data from other sources. The authors classified intrinsic value as: a) high value; b) relative value; c) doubtful value; d) no value; and e) unacceptable value. The expected degree of use was also examined. The criteria for this were: a) high potential for use; b) relatively high potential of use; c) limited potential of use; and d) not considered. All specialities were assessed and classified according to the above criteria by a panel of 5 clinical pharmacologists who were blind about the sales volume of each product. Decisions were taken by consensus.

The results of this study suggest that this type of analysis may be a useful tool to evaluate the efficacy of drugs in the community, and to identify priorities and guidelines in the selection of drugs in each country. The authors conclude that it would be naive to conclude that rationalization of supply of drugs by eliminating irrational, inactive and unacceptable drugs would reduce the pharmaceutical expenditure. They expressed their belief that regulatory restrictions by themselves can do little to improve the use of drugs. Only by a combination of regulatory, informative and educational actions, together with a general improvement of the quality of outpatient medical care in the Spanish National Health system, which is in the main responsible for drug prescriptions, can the use of drugs be more rational.

2.3.5.5 Israel

Antibiotic use on the surgical services of two Jerusalem hospitals, as determined by a surveillance and influenced by an intervention program is reported by Shapiro et al (1981). The use of antimicrobial drugs in the surgical services of two hospitals in Jerusalem, Israel was surveyed prospectively.

2.3.6 Australia

The background of drug usage in Australia is reviewed by Wade (1976). The pattern of drug usage by urban populations was studied in two typical Australian cities: Traralgon, Victoria, and Sydney, New South Wales. The study lasted one year and involved questioning 10% of the residents in households selected by random sampling and records of pharmacists. Questions related to state of health, recurrent or chronic disability, and drug exposures during the two weeks preceding the interview. The data base included the Pharmaceutical Benefit Scheme (a system of partial federal subsidy described later) and the Morbidity Survey of the Royal Australian College of General Practitioners.

The Australian system is further described by Hall (1984). Drugs prescribed by medical practitioners in Australia are dispensed through two major outlets: retail pharmacies and hospitals. The use of drugs in hospitals cannot be monitored in any systematic way on a national basis. However, the use of drugs released through retail pharmacies can be reviewed on a national basis by virtue of the mechanisms by which drugs are made available in Australia.

There are two categories of availability: drugs with general marketing approval; and those which are also available on the Pharmaceutical Benefits Scheme (PBS). In the case of the former, the patient pays the full cost of any drug prescribed, while the drugs in the latter category are subsidized by the Commonwealth of Australia.

The drugs listed in the PBS are described in a handbook which is produced three times a year. Within the PBS there are two levels of subsidy: full subsidy for pensioners, and variable subsidy for the general population who pay a fixed contribution which was $3.20 per item at the time of the paper. The direct consequence of this subsidy is that drugs which are on the PBS account for 90-95% of prescriptions dispensed in retail pharmacies. Drugs in the PBS are controlled at three levels: a) non-restricted benefit: the drug can be prescribed for any indication; b) specified purpose restriction: the specified indications for which the drug should be utilized are specified in red in the prescribing handbook; and c) authority restriction: a drug is available for specified indications as in (b), but application must be made to a Commonwealth office before the prescription is released through a retail pharmacy to the patient. If the proposed use is not precisely as laid down in the pharmaceutical handbook, the application will be refused. An independent committee, the Pharmaceutical Benefits Advisory Committee, makes recommendation to the Minister of Health on listing, restriction, or delisting of drugs on the PBS.

General practitioner prescribing habits in Australia are discussed by Watson and his colleagues (1975). The Australian General Practitioner Morbidity and Prescribing Survey is a continuing research project conducted jointly by the Research Committee of the Royal Australian College of General Practitioners and Intercontinental Medical Statistics (IMS), which provides information about general practitioner prescriptions and the diagnoses for which these were issued. The basis for recording is a triplicate prescription with an added space for the prescribing doctor to record the age and sex of the patient and the diagnosis of the condition being treated. The diagnoses are recorded under a numerical list based on the International Classification of Diseases.

The impact of government controls in Australia on psychotropic drug dispensing between 1967 and 1977 is discussed by Mant and Hall (1982). Trends in the dispensing of three groups of psychotropic drugs are discussed.

Drug usage in a Western Australian rural community is reviewed by Maddison et al (1979) who conducted a study to evaluate the effects of age and possible disease on drug utilization. Drug usage in two agricultural shires, Kondinin and Kulin, was surveyed by questionnaire. Both prescription and over the counter drugs were recorded together with age, sex, forced expiration volume in one second, systolic blood pressure, and body weight.

2.3.7 Third World and W.H.O.

The topic of drug use in the Third World is discussed in a Lancet (1980) editorial. A study of outpatient prescribing in the national teaching hospital in Nairobi, Kenya (Maikai and Watkins, 1980) revealed that multivitamin tablets, chlorpheniramine and Actifed syrup were three of the most commonly prescribed drugs.

The most frequently used eye ointment contained a steroid and one of the most commonly used analgesics contained dipyrone which produces agranulocytosis (Huguley, 1964) and has therefore been withdrawn from the market in developed countries. Furthermore, 44% of prescriptions were for three or more drugs.

Such inappropriate prescribing is not unique in Kenya. In a health centre in Ghana the average prescription contains 3.9 items (Barnett et al, 1980) and it was estimated that "best practice" prescribing could save 75% of the drug budget.

In Tanzania, 10% of outpatients at the national teaching hospital received a benzodiazepine which with thioridazine and two brands of dipyrone were among the hospital's top twenty drugs. The cost of treating a patient was six times greater in the national teaching hospital than in the average hospital, mainly as a result of prescribing expensive non-lifesaving drugs.

The annual drug expenditure in 1975 per person was between 50 pence and 75 pence in these three countries compared with about 9 pounds in the United Kingdom. The prescription of expensive or unnecessary drugs for one patient means that other patients may not receive any drug at all. As hospitals in urban areas tend to be given priority in drug allocation, people living in rural areas may be forced to go without any drugs for long periods.

In India only 20% of the population is believed to have access to modern drugs, while large sections of the rural population are totally deprived (Agarwal, 1978).

The World Health Organization has estimated that 60 to 80% of the population of many developing countries do not have constant access even to essential drugs (WHO,1980). Since drugs are prescribed by health workers, we must look to health workers for improvements in prescribing. An "antibiotic mentality" pervades medical thinking and much of medical education.

Most of the drugs used in the Third World originate from the major western pharmaceutical companies and are promoted vigorously. In Tanzania there is one drug representative for every four doctors, in Mexico one for every three doctors, and the information provided by the representatives in printed material is often incomplete and sometimes misleading (Silverman, 1976 and Medawar, 1979).

An essential drug list based on generic nomenclature has been adopted by many countries in order to remove expensive and unnecessary preparations from both public and private sectors. For example, expenditures on vitamins represents 13% of the drug budget of Pakistan and 8% of that of Venezuela and the Philippines (Tiefenbacher, 1979).

Part of the drug budget in Equador goes on expensive, non-essential or unsafe proprietary medicines, while many drugs considered necessary in developing countries are unavailable (Johnston, 1980). The promotional activities of pharmaceutical companies appear to be unchecked, and objective drug information is scarce. The morality of pharmaceutical companies in developing countries is again questioned in this article. The products which are promoted, the methods of promotion and the negative impact on health and finances in developing countries is discussed. Based on WHO data and sales figures for different countries, Yudkin (1984) also questioned the need for controls on the activities of the pharmaceutical industry and a need for change in medical attitudes.

Rabin and Bush (1974) present an historical review of the development of current levels of medicine consumption with a literature review of cross-national and limited surveys and national statistics on rates of medicine use. Medicine use has increased worldwide at rates exceeding increases in national income in many countries. Variations and estimates of medicine use are documented by cross-national data and expenditure, with prescription rates adjusted to increase comparability. Differences in levels of use appear greater than can be accounted for by methodological problems in comparison.

That differences are great is supported by the results of the WHO International Collaborative Study of Medical Care Utilization (WHO/ICS-MCU in Rabin, 1972) which indicate that age-sex standardized medicine use rates developed from a household survey in twelve areas of seven countries show several-fold differences in rates of prescribed and nonprescribed medicine use. Differences in these rates are not explained by area levels of morbidity or variations in physician visiting or prescribing patterns. Areas tend to be high or low in rates of use of both prescribed and nonprescribed drugs. Problems in the use of data for international comparison of medicine use are discussed.

The major element of this report, the WHO/ISS-MCU, was the household surveys carried out among geographically defined populations of twelve areas in seven countries of North and South America and Eastern and Western Europe during the year 1968-1969. In Canada the areas were: Grande Prairie, Alberta; Saskatoon, North Battleford and seventeen rural municipalities in Saskatchewan; and two areas in British Columbia (code named Jersey and Fraser). Northwestern Vermont and Baltimore Standard Metropolitan Statistical Area were the United States areas; and the Federal District of Buenos Aires was the area selectd in Argentina. European areas were: the Liverpool Hospital Region in the United Kingdom; Helsinki metropolitan area in Finland; Lodz province in Poland; and the Banat and Rijeka regions in Yugoslavia. Respondents were asked about two day use of medicines enumerated by categories and whether medicines used were prescribed or nonprescribed.

Concern about the high impact of drug costs on developing countries and the need for those countries to have a minimum list of effective medications appropriate to the needs of their society, has led to the consideration by an expert committee at the WHO of "essential" drugs for use in developing countries. The assumption was that organized procurement and use of such a limited number would have advantage in terms of economy and effectiveness.

The expert committee expressed concern that many pharmaceutical products are marketed with little concern for the differing health needs and priorities of individual countries. Promotional activities by the manufacturers have created a demand greater than the actual needs. Despite the great increase in drug usage there has not been a proportionate improvement in health. The increased expenditure on drugs in developing countries has led to reduction in funds available for other areas of health care.

The committee decided to select the drug, pharmaceutical product or dosage form with the highest benefit/risk ratio among those available. If two or more drugs were considered therapeutically equivalent, preference would be given to the one most thoroughly investigated, with the most favourable pharmacokinetic properties, for which local reliable manufacturing facilities exist, and with good stability in local conditions. When therapeutically equivalent, cheaper generic products should be used rather than more expensive proprietary products. Fixed-ratio combinations were acceptable only if well justified clinically, if the therapeutic effect is greater than the sum effect of each, if the cost of the combination is less than sum of the individual products, if patient compliance is improved, and if the ratios provided are appropriate to the needs of the population.

Cost was an important selection factor, but the cost of the total treatment rather than the unit cost alone was the dictating factor. The expert committee was able to narrow down to about 200 active substances the drugs considered indispensable for a population's health care. There have been serious criticisms from drug manufacturers who wish to see the use of the essential drug list confined to less developed countries if it is to be used at all.

Manufacturers have been concerned about the suggestions from Norway, Italy and the WHO itself, that such lists might be of value in developed countries. A Lancet editorial (February 25, 1978) called on the British National Formulary to consider modifications which would provide more advice to doctors on drugs to use, how to use them, on their potential dangers and on necessary precaution.

3. FACTORS AFFECTING UTILIZATION (Patterns of Drug Use)

In most western industrialized countries, there are both variations and consistencies in the patterns of use of drugs and medicines. The influences on utilization have been defined by social scientists as cultural heritage, socio-economic class, ideology, education, vocation, age, sex, residence (rural vs urban), neighborhood, family structure, individual attitudes and personality.

In a relatively recent publication reviewing the literature on factors affecting individual use of medicines, Blum and Kreitman (1981) comment that:

> although sophisticated research, be that found in epidemiology, cultural medicine or medical psychology, does demonstrate the complex multi-determined nature of events leading to the use of medicine, such studies are few and far between.

They reviewed several thousand titles and narrowed the relevant publications to just under 200, and were reviewed under the following headings:

- Statistics
- Consumers and Medicine
    - Self-medication
    - Information and Education
    - Sources of Information
    - Consumer Advertising
    - Information vs. Regulation
    - Patient Compliance and Medicine Regimen
    - Determinants of Compliance
    - The Clinical Pharmacist

- Physicians and the Prescribing of Drugs
    - Physicians' Prescribing Habits
    - Psychotropic Drugs and Over-prescribing
    - Advertising to Physicians
    - Generic Prescribing and Consumer Savings
- The Personal Context of Use of Medicine
    - Assumptions and Evidence

Under this last section the authors review the evidence to evaluate a number of commonly held assumptions about the operation of the health care system in society and particularly about the role of the use of drugs and medicines. The assumptions that they analyze are the following:

a) When people report their symptoms to their physician, he makes an accurate diagnosis and prescribes drugs solely on the basis of that diagnosis.

b) When people are ill, they normally consult a physician.

c) The most appropriate and desirable model of the physician-patient relationship is that of a physician (expert) authority figure and a compliant (passive) patient. Patients obey the physician's orders and get well.

d) Humans conform to the rational consensus.

e) Major inroads have been made in eradicating disease among the human population; disease is ultimately conquerable through surgery and drugs. Success only requires that patients visit the doctor and do what he says.

This review of the literature reached a number of important conclusions about the significance of existing data. Before presenting their conclusions, however, they make an important general observation that:

> The scientific literature on factors influencing the use of medicines by individuals is limited to technologically advanced countries, and to populations with access to medicines and physicians in less advanced nations. There are but few studies with data to assist our understanding of medicine use by populations who rely entirely on folk medicine or manufactured pharmaceuticals, dispensed without qualified medical or pharmacists' advice.

For our purposes, however, and with these general limitations in mind, the conclusions of the Blum-Kreitman (1981) report are of considerable interest. Their observation on the available data suggests that:

a) Even in advanced nations, much of what physicians define as illness goes unseen by physicians, but is self-treated through home remedies and self- or family-guided drug purchases. Many of these remedies may be ineffective; some are pallatives, some may be 'curative'. The factors which influence the choice of these remedies are primarily matters of folk culture. Essential to these are personal and family definitions of health and illness.

As with health *per se*, much medicine use is beyond the direct influence of medical care systems or health providers. This is obvious in prescription compliance as well as in self-medication or folk healing. Experts may define the use of medicines as a public health domain, but it is, in fact, a personal, family and peer affair. Insofar as medicine use is externally affected, it is regulatory policy or economics more than medical admonitions which will be dominant.

b) While economic waste is evident and some toxic outcomes are observed, there is no evidence for great threats to public health from existing patterns of self-medication. The significant exceptions are in the cases of drug abuse, i.e. alcohol and tobacco or opiates which are used in a fashion contrary to already existing consumer wisdom and folk norms.

c) Much of what physicians do by way of pharmacotherapeutics fails to conform to present standards of high quality care. Over prescribing appears to be the most egregious error; and diagnostic failure with prescription error is common. If one requires, as a standard of care, sophisticated knowledge about patient behaviour as people (i.e. knowledge of the correlates of common behaviours such as non-compliance to doctors' behaviour and information-giving), then the majority of physicians, especially those engaged in treating ambulatory patients, seem inadequately informed. An unknown, but undoubtedly large, number of these perform inadequately in prescribing.

d) Education and information do have an impact on both physician and consumer, but these influences are exaggerated as "cures" for the various problems in medicine prescription or use. The concept of the rational man or woman, be that doctor or patient, has limited, albeit important, applicability. Thus, the efficacy of information cannot be assumed, although there is no evidence as yet as to "dangerous side effects" from being informed - contrary to the conviction of more paternalistic practitioners. One cannot, however, rule out anxiety as a consequence of information and as a subsequent disruption of behaviour. On the other hand, the same anxiety can be helpful as a stimulus to action, if social supports and clear directions for appropriate action exist to channel it.

e) Given numerous failures in programs designed to recruit patients to medical care, to produce better compliance, to enhance medical care quality, and to reduce unwise drug use, it is apparent that programs for voluntary change involving significant resources or expectations should not be undertaken without prior research, including field evaluations of pilot or test programs. There will be circumstances in which public health can be rather quickly assisted by policies which do not rely on voluntary behaviour, as for example, regulations which remove or restrict access to hazards. Such controls may themselves have negative aspects so that here, too, cost-benefit estimates, pretesting, and a salutory reading of history are in order.

f) In policy and consumer literature, much emphasis is placed on economic forces. This prominence is much more pronounced on the part of interest groups seeking to influence individuals than within the hierarchy of factors identified as salient for individuals themselves. Thus, the profit making on the part of advertisers and economic considerations on the part of governments or labour force productivity interests can be strong forces seeking to affect what the medicine user does. On the other hand, the individual seems relatively indifferent to economic self-interest, getting best buys, avoiding useless products, and insisting on generic drugs when it comes to accounting for what action is taken in regard to the choice and use of medicines. This observation of minimal economic influence is, no doubt, restricted to ceilings on costs and purchases; these being explicit in family budgets or built in by health insurance or medicine cost control policies of health services.

g) The literature on drug utilization has been inconclusive. Consequently very little changes in social policy have resulted. Such proposals, as are commonly made, derive from connections based on more general opinions, as for example, those dealing with medical care quality, epidemiology, resource allocation or other economic ideology or morals. Examples of the latter are those which may condemn advertising for being self-interested persuasion rather than scientific education for physicians and consumers.

Perhaps the lack of consciousness, either about problems or directions, may be attributable to the generally limited or poor quality of research, to the demonstrated complexity of human health/medicines behaviour or to a current awareness that the prediction of the effects of programmed change is rather less easy than one (whether idealist, clinician, or scientist) had initially anticipated.

There are numerous proposals for policies on medicines designed to influence individual conduct. They include: those advocating consumer education; closer scrutiny of physician prescribing; controls over advertising; greater availability of generic drugs; improved pharmacologic teaching for physicians; greater regulation of access to drugs; training physicians in relationship management and patients in communication; or creating in consumers a new role concept of the patient as a decision-making partner in treatment. These and other proposals are each reasonable, yet none are incontrovertibly proven as both necessary and cost-effective.

4. PATTERNS OF EXPENDITURES ON DRUGS

Unfortunately, the literature on the patterns of expenditures on drugs is rather limited and diffuse. While there are "lists and pieces" dealing with expenditures on drugs in various parts of the world, there is no one centralized source of standardized data for all countries. Nor have we been able to find any study which deals with this topic, even at a particular point in time.

Fortunately, however, there are reasonably good data for certain specific countries. Data for the United States are published regularly, and fairly currently, by the National Center for Health Statistics (Public Health Services Department of Health and Human Services of the U.S. Government) in a publication called Health - United States. It is published annually and provides statistics for the previous fiscal year. The series started in 1976 and the most recent report is for 1985.

Data on drug use and expenditures are presented in a variety of ways. These include national health expenditures and percent distribution for the period from 1950 to 1982. The data are further presented by the average annual percentage change of each category of expenditure.

Similar, and almost comparable, data are published by the Health Information Division of the Policy, Planning and Information Branch of the Department of National Health and Welfare of the Government of Canada. These data are published under the title of

National Health Expenditures in Canada, the latest publication being for the period 1970-1982. Fortunately, the Health Information Division is currently in the process of compiling an update of their National Health Expenditures series for the period 1975-1985, and has prepared "pre-publication" tables which have been made available to a small group of interested people. Thus, data regarding drug expenditures in Canada are available for the period through 1985.

The Canadian publication provides a broad range of health expenditures data, both on the basis of total national expenditures as well as by province. Health expenditures are separated into categories, of which one major category is "Drugs and Appliances". This is further broken down into: prescribed drugs, non-prescribed drugs, eyeglasses, hearing aids, and health appliances and other prostheses. Thus, we are able to identify drug expenditures separately from appliances, and even separate expenditures on drugs into prescribed and non-prescribed. The data are further analyzed by percentage increases over previous years, expenditures per person, the distribution of expenditures by percentages associated with each category, and the percentages of the gross national product associated with each category of expenditure.

The publication also contains a section reporting on health expenditures in the United States. This follows a format similar to that used to report Canadian data and thus, to some extent, comparisons can be made between the two countries. Unfortunately, the categorization of expenditures on drugs and appliances is different between the two countries. The U.S. drug expenditure data is not broken down into prescribed and non-prescribed, and appliances are grouped somewhat differently from the Canadian categories. Therefore, while general comparison can be made, more precise analysis is difficult and is influenced by a variety of assumptions. Despite these limitations, however, the data are valuable and substantially better than those available for other countries.

The Canadian data most relevant to the study of drug utilization are those dealing with expenditures on drugs, increases of expenditures over previous years, expenditures per capita, drug expenditures as a proportion of all health expenditures, and percentages of gross national product. The comparative data for the United States, recognizing the limitations imposed by differences in definitions, also are of great interest.

Of particular significance is the fact that drugs now represent a larger proportion of health care expenditures than previously, and prescribed drugs have been consuming an increasing proportion of health expenditures during the past six years. It also is significant that the percentage increases over previous years for expenditures on prescription drugs for the past five years have been consistently higher than increases on health expenditures generally, and in some years considerably higher. In 1981, for example, prescription drug expenditures increased 27.66% over the previous year as compared to 17.47% for personal health care expenditures generally. For 1985, the comparable figures, although provisional, amount to 13.0% and 6.67% respectively. Thus, expenditures on prescription drugs represent an increasing proportion of our health care expenditures.

Comparing Canadian expenditures with those in the United States presents some interesting differences. Percentage increases in expenditures on drugs and appliances over the previous year are illustrated in Figure 1.

Drugs and appliances as a proportion of total health care expenditures and as a percentage of gross national product of the two countries are shown in Figures 2 and 3 respectively.

Although there are no central sources of drug expenditures data for all countries in the world, periodically there are reports for certain selected countries. For example, the Commonwealth Pharmaceutical Association published in 1985 the study, Pharmaceutical Manufacture and Formulation in the Commonwealth, in which they reported on drug expenditures in 44 countries. The importance of the study, in addition to providing data which were previously unavailable, is to recognize the huge variance in per capita drug expenditure among the different countries. Since so many of the countries are classified as "low income" or "lower middle income", the level of their expenditures on drugs is very significantly lower than that in higher income countries. As a matter of fact the per capita expenditures vary as much as forty-fold.

Another example of international comparisons is the reported number of drug products available in various countries throughout the world (see Table 1). This shows the tremendous variation in the number of different drugs available in different countries.

Figure 1: DRUGS AND APPLIANCES
PERCENTAGE INCREASE OVER PREVIOUS YEAR

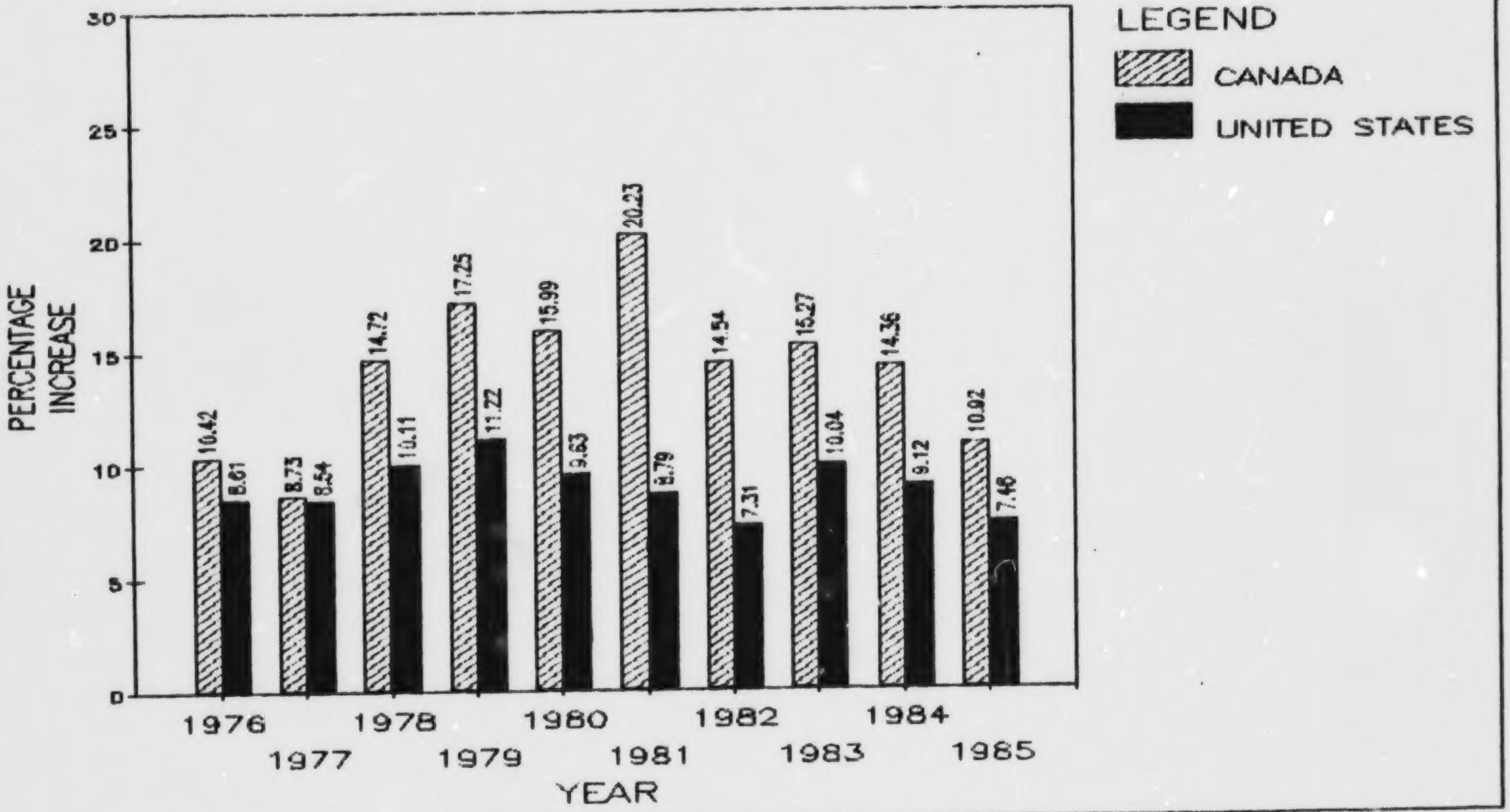

Figure 2: DRUGS AND APPLIANCES
PERCENTAGE OF
TOTAL HEALTH EXPENDITURES

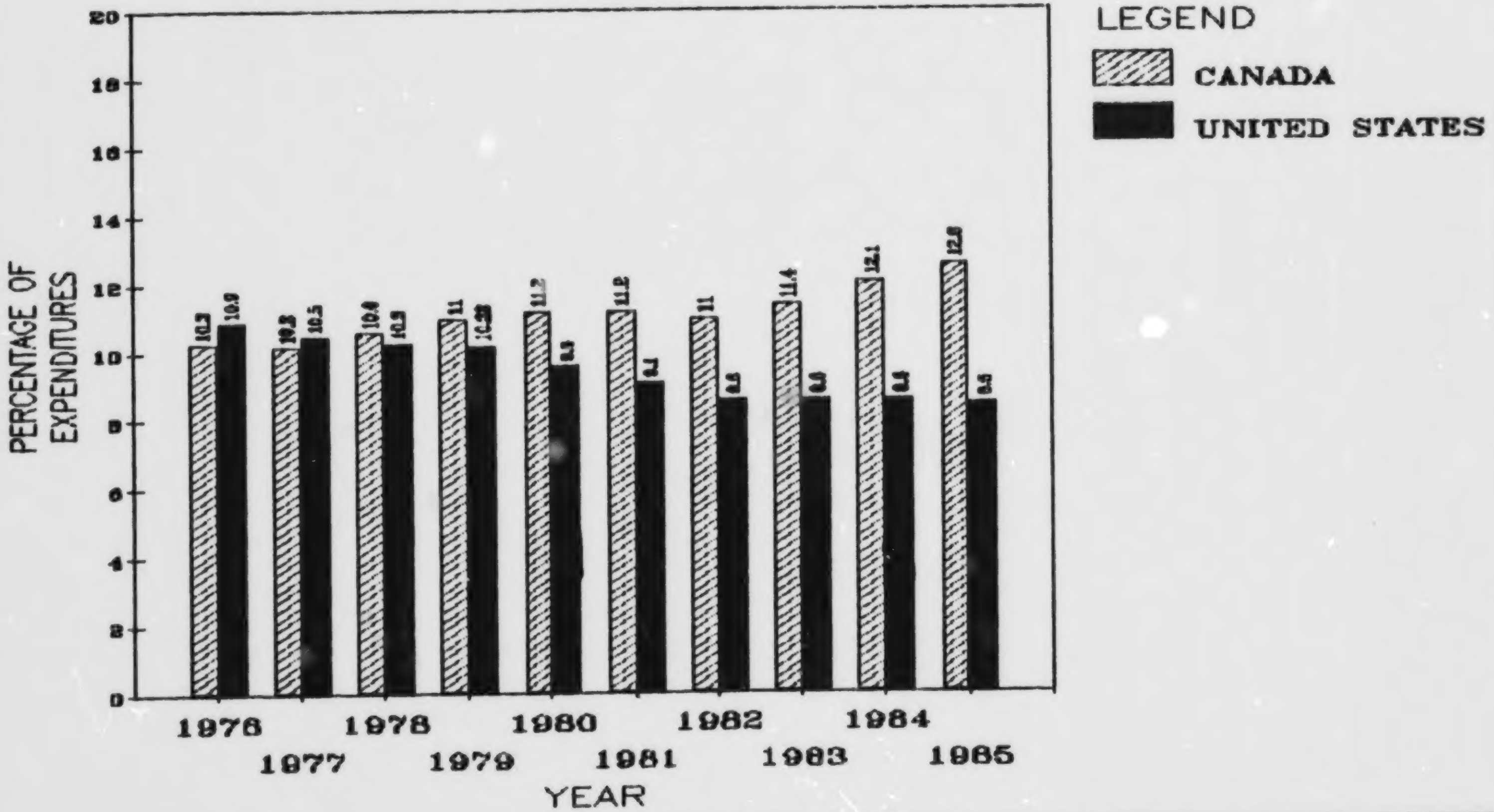

Figure 3: DRUGS AND APPLIANCES **PERCENTAGE OF GROSS NATIONAL PRODUCT**

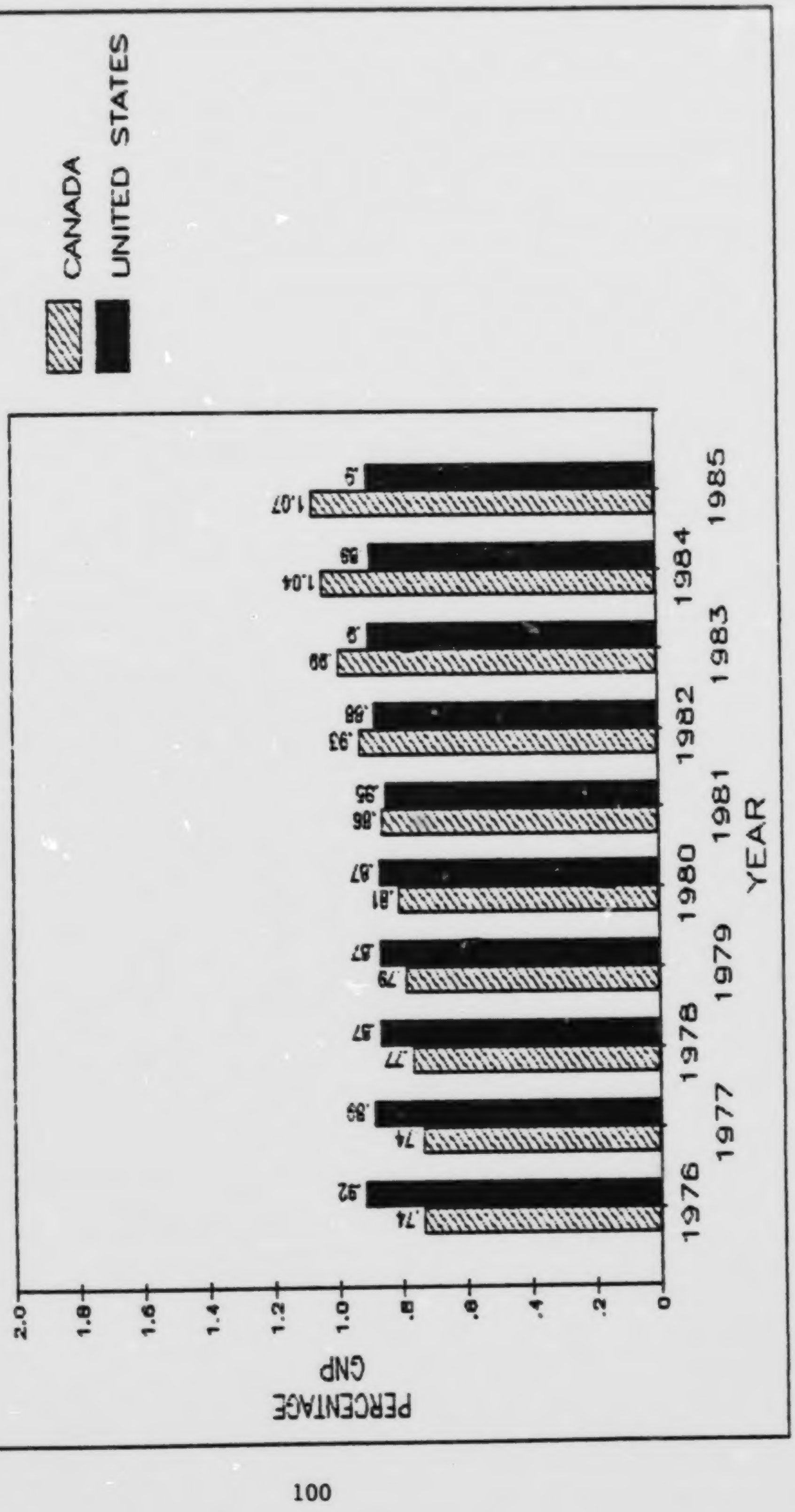

Table 1: Estimated Number of Presc ption Drugs (Products) Marketed in Selected ountries

Country	Numbe of Drug Products
United Kingdom	15,000*
West Germany	15,000*
Italy	13,700*
Japan	16,600+
United States	12,500+
Canada	12,000+
Switzerland	8,900+
Greece	8,000+
Belgium	7,900*
France	7,800*
Ireland	7,400*
Luxembourg	7,300*
Australia	7,000+
Finland	3,700*
The Netherlands	3,400*
New Zealand	2,900+
Sweden	2,700*
Denmark	2,100*
Norway	1,900*
Iceland	1,100*

Source: Reported in Silverman, Lee and Ly cker, *Pills and the Public Purse*, p.139. It identifies numbers m ked with a plus (+) are semiofficial governmental figures. Nu bers marked with an asterisk (*) are taken from M.N. Graham D es and Inga Lunde, "Controls, Common Sense, and Communities", *P rmaceutisch Weekblad* 114:1283 (1979); and Dukes and Lunde, "Measuri the Effects of Drug Control - An Emerging Challenge", *Pharmace ical Journal* (London) 223:511, Nov.17,1979.

5. ROLES

The use of drugs varies considerably, both by groups inside the country as well as in comparison between and among nations of the world. Factors that are associated with differences in drug utilization are age, sex, insurance status, ethnic and cultural background, income, etc. Variations among countries include both the numbers and types of drugs available as well as costs and expenditures on drugs.

This review is concerned only with the utilization of legend drugs, those requiring a prescription for their being dispensed. However, it is recognized that there are similar variations in the patterns of utilization and costs of non-legend or 'over-the-counter' drugs, which do not require a prescription for their purchase.

There are a wide range of influences within society that affect the amount and patterns of drug utilization. These include: a) the prescribers (physicians and others legally authorized to write prescriptions); b) the dispensers (pharmacists and others entitled to provide the purchaser with the final product); c) the patient for whom and to whom the process is directed; d)the drug manufacturer (who represents an industry which is large, profitable, powerful and internationally integrated); e) the regulators (government and third-party payors who have a stake in promoting more rational and more efficient utilization of drugs); and f) the environment (meaning mainly the media) which influences not only the public awareness of the availability of particular products, but the desirability of utilizing the products advertised. Each of these various "actors" has profound influence on the amount and patterns of drug utilization. And each requires careful review to determine its influence on the utilization of drugs in our society.

The need for the study of drug utilization practices is based on the increasing evidence of irrational prescribing, drug waste, and misuse of medications by patients in both private and public health care programs. Many studies have documented the irresponsible prescribing of certain medicines, such as proprietary analgesics, psychotherapeutic agents and expensive antibiotics, without establishing any acceptable justification for their use. Other studies have demonstrated equally irresponsible practices such as the prescribing of excessive quantities of drugs, or the collection of multiple prescriptions from different physicians for the same symptom. Reports of large quantities of unused medications in patients' homes also indicate wasteful and costly drug utilization practices.

This study, then, reviews the literature on the influences of the various factors on drug utilization and the costs associated with it.

5.1 Role of Physicians

Considerable attention has been paid to the role physicians play in the large, and increasing, consumption of drugs in all Western countries, if not throughout the entire world. Whatever the causes for the great growth in drug utilization, it is obvious that physicians must play a significant role in this development, since it is they who control access to legend drugs by the possession of a virtual monopoly on the right to issue a prescription for the dispensing of such drugs.

There have been many attempts to try to influence physicians to be more rational prescribers. In a review article, Hemminki (1975) surveyed the variety of influences that bear upon physicians in the process of writing prescriptions. The influences identified were: education, advertising, colleagues, control and regulation measures, demands from society and patients, and doctors' characteristics.

The conclusion drawn by Hemminki, after reviewing more than seventy studies mainly in Britain and the U.S., is that "the knowledge on the factors affecting drug prescribing is limited, at least in the medical and scientific literature. It is possible that more accurate knowledge exists in sources not freely accessible to investigators, e.g. in drug firms".

A more recent report by Soumerai and Avorn (1985) provides a more optimistic note on the possibility of improving prescribing appropriateness by physicians. They report the results of an experimental educational outreach program designed to reduce inappropriate drug prescribing. Primary care physicians were offered two individualized educational sessions with clinical pharmacists, lasting an average of 18 minutes each, concerning optimal use of three drug groups that are often used inappropriately. After the program, expenditures for the target drugs prescribed by these physicians to Medicaid patients decreased by 13%, compared with controls; this effect was stable over the period of the study. The net effect of extending such a program to large numbers of physicians would result in substantial savings over costs.

A much more pessimistic view of our ability to control irrational prescribing by physicians is expressed by Lee (1980) in his article "America is an Overmedicated Society". Lee's conclusion is that indeed the United States and Canada are overmedicated societies. He provides a somewhat greater analysis of the problems associated with the obstacles to rational prescribing by physicians in the book which he co-authored with Silverman and Lydecker (1981) called Pills and the Public Purse. There he identifies a number of problems causing irrational prescribing as follows:

a) the inadequate training of physicians during their medical school years on the day-to-day application of drug knowledge;

b) the inadequate sources of objective information available to practicing physicians about drug properties and indications;

c) the widespread custom of physicians to continue their drug education by relying mainly on the promotional activities of the drug companies;

d) the exceedingly rapid turnover in the popularity of prescription drugs; and

e) the limited time available to practicing physicians to study and evaluate the therapeutic claims for newly marketed drugs.

In discussing how we can achieve more rational prescribing Lee identifies the need to proceed along a number of different lines. He proposes:

a) that physician education be improved;

b) that the information available to practicing physicians be vastly enhanced, hopefully with the preparation of a complete drug compendium, updated at reasonable intervals;

c) that hospitals and their medical staffs accept greater responsibility by upgrading their efforts in clinical pharmacology, and in providing greater leadership in continuing education of physicians, particularly in the area of drug prescribing and drug utilization;

d) that drug utilization review systems be more widely applied; utilized; and finally, and perhaps most significantly,

e) that greater emphasis on governmental approaches be given to the review and regulation of many aspects of health care, including the use and misuse of prescription drugs.

Rabin (1974), another prominent writer in the area of drug prescribing and utilization, reviewed the literature in regard to the factors associated with better prescribing. His review identifies the following factors as being associated with better physician prescribing: younger age; specialization (particularly in internal medicine); more pharmacology teaching; health maintenance organizations (HMOs); group practice, and urban locations.

According to Rabin, it is impossible to determine the absolutely appropriate level of prescribing. However, there is little doubt that there continues to be problems in prescribing.

> These problems relate both to over prescribing of drugs like antibiotics for conditions like the common cold, as well as under prescribing of preventive medications like vaccines for unimmunized children and adults. As knowledge of the risks associated with the taking of certain medications increases and the efficacy of taking other medications is increasingly apparent, there should continue to be changes in prescribing patterns. Inevitably these changes will occur with some delay from the time that there is medical consensus that a particular pattern of prescribing is more appropriate.

5.1.1 Defining Rational Prescribing and the Physician's Role

The World Health Organization has also been concerned about how to make the prescribing of drugs more appropriate (WHO, 1986. Report of the WHO workshop "Medical Education and Rational Prescribing of Psychoactive Drugs" St. George's Medical School, London, September 15-19, 1986). Considerable evidence exists that through over-prescribing important public health and social problems occur, e.g. abuse and dependence (Shader and Greenblatt, 1984). The term 'rational prescribing' has become the verbal shorthand to describe what is desirable.

The goal of all prescribing is ideally optimal therapy and rational prescribing is essential to reach this goal. Unfortunately, rational prescribing cannot be defined simply, because what is 'rational' is determined by many factors. What is 'reasonable' to the patient, physician, insurer, politician, administrator, economist, manufacturer, distributer, pharmacist and the public can be quite different. These views are modulated by cultural, social and economic factors, population health status, and prevalent forms of health care delivery in particular countries. In addition, prescribing patterns are affected by drug marketing legislation, patent laws, international conventions, methods of health care insurance, method of pharmacist payments, and existence of drug formularies. Rational prescribing can be pointless if patient compliance is low. Patient compliance is affected by health beliefs and behaviours, disease and drug cost (Wardell, 1978).

Notwithstanding these factors, the physician ultimately controls the prescribing of a drug. Thus, the issue ultimately focuses on him or her. Contextual factors must be accepted as important but constant in each setting. The problem of defining rational prescribing and reaching an operational definition can be handled by identifying components of the process of rational prescribing. Rational prescribing may be achieved by a systems approach which links the prescribing behaviours of individual physicians to features of the health care system which encourage rational prescribing. Features of the health care system which may encourage rational prescribing include: drug availability, drug use monitoring, prescribing standards, drug use audit, feedback and education of individual physicians, and monitored patient health outcomes.

5.1.2 Rational Prescribing by the Individual Physician: the Step Care Therapeutic Plan (see also Table 2)

Physician prescribing is a complex behaviour incorporating knowledge about drug availability, pharmacology, use, and toxicity and skills in the therapeutic use of the drug. The step care therapeutic plan for physicians to achieve rational prescribing includes:

a) Diagnostic certainty. The individual physician must have sufficient evidence to support a diagnosis. Under acute emergent situations a presumptive diagnosis may be acceptable, but in all other situations investigation should be completed before treatment is initiated. Often this information requires a combination of spontaneous and elicited signs and symptoms using validated clinical scales.

b) Specification of an overall treatment plan prior to prescribing a drug. The plan should include all elements of physical, psychological, social, educational, recreational, family and pharmacologic therapy.

c) Specification of short term and long term treatment outcomes.

d) Drug selection based on scientific proof of efficacy in the diagnostic patient group. The drug's relative safety, initial dose, prescription size and planned duration of therapy should be known. Whether only the most efficacious, safest and cheapest drug should be prescribed is a moot point. Often such comparative information is not available.

e) Skilled therapeutic use of psychoactive drugs. A physician should be skilled and experienced in the use of drugs. This presumes formal training in their use at some point. Prescribing for unapproved or scientifically unsupported indications or in dosages different from those recommended or for durations longer than proven to be effective should probably be confined to designated specialists with extensive experience.

f) Monitoring the patient's response at appropriate intervals to ensure a response is obtained. Drug dosage should be adjusted within scientifically or peer-consensus recommended dosage schedules on the basis of clinical response, or by using indirect laboratory tests (e.g. drug concentration measurement in prophylaxis). Therapy should be continued only for the usually recommended duration of known effectiveness.

These criteria may be thought of as too rigorous and beyond the 'state of the art'. For example, it may be suggested that criteria for establishing the efficacy of psychotropic drugs do not exist and that psychiatric diagnostic criteria are too vague. The whole basis of drug approval and indication labelling in most countries is based on the assumption that there has been a scientifically objective demonstration of efficacy. Hence, the task is not impossible.

The educational implication of this step care therapeutic plan is that the graduated physician should have the necessary attitude, knowledge and skill to follow the plan. Evidence exists that the amount and form of current information falls short of what is needed (Sellers et al, 1987).

5.1.3 Rational Prescribing in the Health Care Field

Extensive evidence exists that local and national drug utilization monitoring systems linking drugs and their actual use are essential if quality drug use is to be achieved (e.g. British Columbia Pharmacare - Canada, Medicaid Management Information System - USA, and Prescription Prescribing Authority - United Kingdom). Many existing drug utilization systems, some quite small, are or can be used for this purpose. Local decentralized approaches are very desirable since they seem effective. Drug utilization monitoring must be linked to review (audit) of the patterns of prescribing. Physician peers and experts prepare relevant (e.g. local, national, etc.) audit standards of rational prescribing for selected drugs and drug classes of concern. Such an audit, using predetermined standards, provides a way of identifying unacceptable deviations in prescribing practices. Information feedback to individual physicians can be coupled with general and targetted educational maneuvers (Melander and Stenberg, 1986). Specific programs can be developed to examine patient outcomes in target populations (e.g. institutional patients) and for target drug groups of special concern (e.g. neuroleptics). The focus of monitoring and auditing can vary, but should continue long enough to establish the effectiveness of each restrictive or educational maneuver. Typically this may be for up to 1-2 years.

With the advent of more comprehensive health care and the extensive involvement of governments, insurers and health care administrators in drug distribution and use, the dimensions of 'rational' must be addressed. Often current drug utilization systems are concerned with cost reduction. In such systems peer and expert standards for prescribing and determining interchangeable products can be used as guidelines to achieve quality care and to reduce cost. However, compliance with guidelines is only an indirect measure of improved patient outcome; hence it should not substitute for direct measures of health status.

5.1.4 Comment

Rational prescribing may be achieved by a systems approach to drug use by physicians and patients in populations. The approach incorporates a coherent series of interrelated components affecting drug availability, drug use monitoring, drug prescribing standards, drug utilization audit, feedback and education, targetted feedback and education for individual physicians, and monitoring patient outcomes.

TABLE 2: EXAMPLES OF STANDARDS OF RATIONAL PRESCRIBING (Rucker, 1971)

1. RELATIONSHIP OF PATIENT CONDITION TO DRUG AGENT PRESCRIBED.
2. EVALUATION OF PRESCRIBING PATTERNS IN TERMS OF THE PROPORTION OF FIRST CHOICE, SECOND CHOICE AND RESERVE CHOICE DRUGS SELECTED BY GIVEN PHYSICIANS.
3. PRESCRIBING OF COMBINATION PRODUCTS.
4. EXTENT TO WHICH GENERIC ITEMS OR HIGH COST BRAND ALTERNATIVES ARE SPECIFIED.
5. MAXIMUM DRUG QUANTITY.
6. MINIMUM DRUG QUANTITY, WHEN APPROPRIATE.
7. MULTIPLE PRESCRIBING, INCLUDING INTERACTIONS.
8. SELECTION OF APPROPRIATE DOSAGE FORMS AND STRENGTHS
9. CRITERIA FOR USE OF NO DRUG THERAPY IN CONTRAST TO THE PRESCRIBING OF A GIVEN MEDICATION.
10. CRITERIA FOR DELAYED DRUG THERAPY.
11. USE OF COMPOUNDED MEDICATIONS.
12. REFILLS - MAXIMUM NUMBER AND AMOUNT OF DRUG SUPPLY IN PATIENT POSSESSION.
13. LABORATORY TESTS (OR SIMILAR PROCEDURES) REQUIRED TO ESTABLISH AND/OR MONITOR USE OF A GIVEN AGENT.

5.2 Role of Pharmacists

The pharmacist is the link between physician and patient in the distribution of medications. In this capacity, the pharmacist assumes a critical role of judgement in the appropriate use of drugs. Lee (1979) has discussed this problem from the point of view of overmedication, which he describes as unjustified or inappropriate drug use. He stresses that physicians, pharmacists and patients must work together in order to deal with the problem effectively. Citing non-compliance as the issue, each of these parties must increase his communication with the other in order to achieve more appropriate drug use. In particular, the pharmacist's role is of value as a drug counsellor because many patients take multiple drugs simultaneously with the potential for adverse effects.

Patry et al (1981) reported on a study that compared drug use investigations conducted by pharmacists and those conducted by physicians. They concluded that there does appear to be a difference in perspective concerning DUR criteria and follow-up measures. The major differences in follow-up was that physicians tended to be more punitive whereas pharmacists favoured an educational approach to achieve the desired change in behaviour. In addition, pharmacists preferred drug-oriented criteria and physicians favoured patient or disease oriented criteria in studying DUR.

Involvement of various health workers (e.g. nurses, pharmacists and physicians) occurs in many cases leading to the betterment of patient care. Drug histories were the focal point of two studies reported by Barger and Barger (1976). In the first study, admission drug histories were taken by physicians, nurses and pharmacists from 50 patients. Those taken by the pharmacist yielded twice as many prescription medications and ten times as many over-the-counter drugs as the histories taken by physicians and nurses. The second study was done with 100 patients on the same medical units and used the same nursing staff as the first study. The main difference was that an admitting note form was instituted for use by the nursing staff three months prior to the study. As a result, questions about allergies and current medications were asked. This study showed a 50% increase in the total number of drugs found and a 3-fold increase in the number of over-the-counter drugs. Thus, the difference in forms appears to be a critical matter in collecting drug use data. Nursing effectiveness increased and the data were available for the pharmacist to monitor.

A later study that looked at physicians, nurses and pharmacists who conducted patient drug histories reaffirms the Bargers' findings. Walchle and colleagues (1980) attempted to determine quantitative differences in medication histories of selected patients conducted by pharmacists, nurses and physicians in a 99 bed community hospital. They found that the hospital pharmacist documented more frequent medication use than the nurse or physician and concluded that the pharmacist is a valuable resource in documenting drug use prior to hospital admission.

5.2.1 Pharmacists' Influence in Prescribing

The role of the pharmacist has increased steadily to the point where a definite influence on drug therapy is noticed. Studying two family practice residency training offices for prescribing patterns, Carter et al (1984) found that the situation where a clinical pharmacist was present contributed to better drug choice and drug dose compared to the site which had no pharmacist.

A study done in the early sixties tends to reinforce the fact that pharmacists influence physicians' prescribing habits. Newman (1961) reported on a nationwide U.S. sample of 3400 questionnaires to pharmacists who dispensed from 0 to 75 prescriptions per day, and who also received the trade magazine, American Professional Pharmacist. Although questionable methodologically, the findings reported that pharmacists who dispense more prescriptions per day believe that they influence a physician's prescribing more than pharmacists who dispense fewer prescriptions per day. The degree of pharmacist-physician interaction also appeared to be related to this ability to influence the physician.

Another study on the influence of pharmacists was reported by Knapp et al (1978). In this instance, the most frequently prescribed drug products were reviewed for existing prescribing and dispensing patterns in ambulatory patients. Eight of the top 25 most frequently prescribed products were considered pharmacologically or therapeutically questionable. Using data from IMS America's National Prescription Audit, they concluded that drug prescribing review and prescriber identification are crucially needed, as well as formulary controls when feasible. They believe that formulary control would be more appropriate for drugs that are pharmacologically irrational and a drug prescribing review would be more reasonable for pharmacologically rational drugs that are used inappropriately. It seems apparent that pharmacists, in this case, were not exercising a therapeutic monitoring or consultative role.

Pharmacist-physician interactions in the selection of drugs for their patients is exemplified in the use of generic products. A joint committee in a Virginia county prepared a list of eleven widely used generic drugs that offered a cost advantage to patients (Kunin and Dierks, 1969). When these drugs were prescribed, the pharmacists passed the savings on to the consumer. Of the recommended generics, prescribing increased from 36.4% before the study to 59.8% and 49.5% three and six months later.

Attitudes of health workers toward one another seems to be an important factor in their cooperation with one another. This was illustrated by Nelson et al (1978) when they examined physicians' attitudes toward pharmacists as drug information consultants. Six areas related to the pharmacists' competencies were investigated: literature reports of clinical studies; drug effects on laboratory tests; drug-drug interactions; adverse drug reactions;

contraindications; and choice of the most appropriate drug. As well as assessing pharmacists, physicians were also asked to rate their own competencies in these areas in a two-phase experiment.

The outcome of this study showed that the physician assessments of pharmacist competencies in all six areas of clinical drug information improved following implementation of clinical pharmacy services, and also reported an increase in frequency of using pharmacists as a drug information resource. Pharmacists were also assessed as having greater competency than physicians in the first four areas of drug information and equal competency in the contraindication area. Physicians, however, perceived themselves to be more competent than pharmacists in their ability to choose the most appropriate drug.

5.2.2 Counselling

The contribution of a pharmacist in monitoring drug therapy goes beyond simply reviewing prescription or drug orders. There appears to be a responsibility to monitor pharmaceutical manufacturers' promotional material. A study conducted in the mid-1970s examined selected antibiotic advertisements in medical journals and illustrated misleading information that was disseminated to physicians about indicators for use and side effects (Hendeles, 1976). Pharmacists have an opportunity to expand their role and provide information to physicians that will help in creating optimal use of drugs by "counter-detailing."

A brief report appears in the pharmacy literature about counter-detailing (Gouveia and Wissinger, 1979). In this example, it is in response to the introduction of two new antibiotics which were heavily promoted, but in fact had only minor advantages over current therapy. They had the potential for increasing drug costs and anxiety that over-use might result in development of organism resistance. The pharmacists in the hospital concerned turned to "counter-detailing" of these agents with the result of limiting prescribing for the new products.

Related to the concept of including new drugs into a hospital formulary is that of deleting older or ineffective products. Lemay et al (1981) has reported a strategy for deleting popular drugs from a hospital formulary. It is basically a step-wise progression beginning with problem identification, literature evaluation, soliciting medical staff support, presentation to the Pharmacy and Therapeutics Committee, creating a timetable, educating users, monitoring use, coordinating activities of the departments concerned, and follow-up where necessary.

As well as providing information to physicians, pharmacists can, and do, provide drug information directly to the patient or consumer. Schondelmyer and Trinca (1983) conducted a study among community pharmacies in Arizona to determine whether consumers wanted this type of service and were willing to pay for it. They found that 36.3% of consumers were willing to, and did, pay for this counselling.

Other studies that illustrate pharmacists' clinical contributions indicate their effectiveness in: reducing drug costs in hospitals (Abramowitz et al, 1982 and Herfindal et al, 1983); altering medication use patterns in a long-term care facility for the mentally ill (Berchou, 1982; Tait and Hall,1978 and Inoue, 1978); decreasing costs, increasing discharge rates, and decreasing readmission rates in an acute adult psychiatric facility (Saklad et al, 1981); providing cost beneficial education and consultation advice by concurrent monitoring of prescribed (selected) antimicrobials (Suzuki and Pelham, 1983); and reduction of drug costs on a cardiothoracic/vascular surgical unit (Herfindal et al, 1985).

5.2.3 Risk Management and Clinical Influence

The resources of clinical pharmacists appears to be a useful addition in a clinical setting. Knapp and Knapp (1979) explain a strategy for increasing the demand for these practitioners. They suggest three steps: a) show that the overall quality of drug prescribing effects patient outcomes not only in a negative way, but also in a positive manner, i.e. appropriate prescribing speeds recovery and minimizes the need for more expensive types of care; b) show that the pharmacist can detect poor quality prescribing; and c) show that after detecting poor quality prescribing, the clinical pharmacist can effectively intervene in the prescribing process to reduce inappropriate prescribing and improve patient outcomes.

Mikeal (1974) has set out a protocol for evaluating the quality of pharmaceutical services in which he discusses the sequence of events to be carried out in this process. The concept of evaluation of any service should not be taken casually, and he points out that if pharmacists wish to increase their professional responsibilities, they must evaluate the quality of the services they provide.

An example of an evaluation process is provided by Guernsey et al (1983) who conducted a 12 day peer-review audit at an outpatient pharmacy of a large teaching hospital. They found that a total of 12.4% dispensing errors, with 1.5% of those considered to be potentially serious. Additionally, there was a linear relationship between the number of potentially serious errors and the total number of prescriptions dispensed. The study concludes that pharmacies with high volumes should set a limit to the number of prescriptions dispensed per pharmacist and should experiment with quality assurance systems to reduce errors.

Carroll et al (1978) examined patterns of use of medication ordered on a PRN basis to determine the effect of such errors on pharmacy workload. They found that drugs in unit dose packaging were returned to the pharmacy unused 79% of the time, and that workloads could be decreased by modifying the amount of medication dispensed for these orders.

As pharmacists become more involved in the drug taking aspect of drug therapy, their use of professional judgement increases. An example of this judgement is the work carried out by Nelson and colleagues (1984) in a Veterans' Administration Medical Center. The major problem in these centers is sporadic medication refill behaviour on behalf of the patients. The cause of this behaviour is thought to be a result of noncompliance, provider misinformation, poor communication, inefficient management systems, and inconsistent delivery of service. The pharmacist's goal is to provide consistent application of the VA regulations for medications and arrange for follow-up care. This takes place in a medication refill clinic where the pharmacist evaluates patients who present themselves requesting medication. Although following a series of protocols, the pharmacist may order laboratory and radiographic analysis. The attending physician of the admission/emergency unit assists the pharmacist in the clinical decision.

5.2.4 Prescribing

From the literature reports, it is becoming clear that pharmacists have increased their influence on the decision process of drug consumption, particularly in a clinical setting. As a result of this role evolution, it may seem reasonable that pharmacists have begun to prescribe drugs. A pilot project allowing pharmacists to prescribe was initiated in California in 1977 (Conte, 1986). However, the initial legislation appeared in December, 1972 which authorized the California Department of Health "to approve health manpower projects sponsored by non-profit facilities. This law allowed project trainees, under specified conditions, to perform health-care services that were beyond the normal scope of their job descriptions". Later, 1977 legislation in California permitted pharmacists to prescribe and administer drugs or devices in pilot projects with specified exceptions. Conte described the programs for these projects which consisted of a training phase followed by an employment phase in which the pharmacists performed under protocols supervised by physicians.

Stimmel (1983) examined the appropriateness of pharmacist prescribing. He considered arguments for and against support of this role. In support of pharmacist prescribing he presents the following: a) in current practice, pharmacist consultation has evolved into prescribing; b) there is a need for pharmacists to prescribe; c) nurse practitioners and physicians' assistants who are trained in clinical pharmacology by pharmacists, have authority to prescribe in many states; d) as the need for dispensing medications decreases, new functions must be assumed; and e) pharmacist prescribing in pilot studies has been safe, effective, and either equal or superior to physician prescribing.

Negative arguments include the following: a) not all pharmacists are competent to prescribe; b) pharmacists are not trained in diagnosis; c) physicians oppose it; d) it could increase patient care costs; and e) pharmacists' access to patient information is not adequate for competent prescribing.

Further, he indicates that legislation regulating pharmacist prescribing should limit the function by: a) certification to prescribe should be based on demonstrated competence; b) pharmacists who prescribe must have access to medical records; c) pharmacists must prescribe within established working relationships with physicians; and d) pharmacist prescribing should be limited to long-term therapy for chronic disease and therapy for acute self-limiting illnesses that are not diagnostically complex.

These limitations have been incorporated into California law. Editorial support and opinion within the pharmacy literature for the concept of pharmacist prescribing is favourable (Lipman, 1982; Perchak, 1983; and Covington, 1983 and 1984) and an evaluation of its effectiveness has taken place in a geriatric setting. Thompson and colleagues (1984) report on clinical pharmacists who, under physician supervision, assumed responsibility for the drug management of geriatric patients in a skilled nursing facility. Using a pretest post-test design, they measured: the outcome criteria of drugs per patient; discharge to a lower level of care; hospitalization of patients; and deaths in the physicians' groups (control) and pharmacists' group (treatment).

The prescribing pharmacists' group had a lower number of deaths, a higher number of patients discharged to lower levels of care, a lower average number of drugs per patient, and a lower hospitalization rate. Based on these findings, the researchers speculate that pharmacists' prescribing has the potential for substantial cost savings in this type of facility.

Similar results are reported by Stimmel et al (1982) who described a study comparing three certified pharmacist prescribers and two psychiatrists in a 40 bed mental health facility in California. Each prescriber had 60 of his prescriptions for previously diagnosed patients evaluated by a panel of four clinical judges. All treated patients were similar in age, sex ratio, number of drugs prescribed, and number of medical diagnoses.

The research found that the appropriateness of pharmacist and physician prescribing to be significantly similar. This tends to be confirmed in a similar study conducted by McGhan et al (1983). In this study, a comparison between pharmacists and physicians was made in prescribing for hypertensive patients. There was no difference between the groups for drug interactions, appropriateness of quantities, dose, and patient directions. Pharmacists, however, did better on selecting the appropriate drug.

5.2.5 Comment

From a review of the literature, the concept of drug utilization review and the pharmacist's role appear to be quite compatible. It is apparent, however, that the pharmacist cannot work or act alone in this capacity as monitor. He/she is seen to be most effective when working with other health professionals, in particular the nurse and physician. As a team, this group of health workers, in communication with each other, are in an excellent position to increase the quality of health care, especially as it pertains to drug therapy.

Because of their knowledge of drugs and biological sciences, coupled with a close contact to the patient, pharmacists are well positioned not only to collect drug histories, but to assess them and recommend changes as required by the patients' response to drug therapy. In addition, more judicious use of drugs often leads to less cost to patients, health care institutions, and insurance carriers.

The evolving clinical nature of the pharmacist's role over the last decade has increased their influence over the procedure of prescribing. As well, responsibilities on formulary committees, active participation in drug information centers, ward rounds, pharmacokinetic consultation services, and increased primary patient-care duties are all extensions of pharmacist roles with implication for drug therapy.

It is interesting to note as Stimmel (1983) has indicated, that these new clinical oriented "roles were not created in a void; instead, these roles emerged in response to a need for services." As a result of acceptance of these roles by other health workers, pharmacists have taken what seems to be the next logical step - prescribing. The pilot programs in California have demonstrated that appropriately selected and trained pharmacists can prescribe rationally or slightly more appropriately than physicians in the same facility. As there is room for improvement in drug therapy for the patient, there is opportunity for pharmacists to bring their particular drug expertise to the fore in order to optimize drug use and minimize drug toxicity.

5.3 Role of Patients

The debate continues about the role that patients play in respect to drug therapy. Regardless of the theoretical arguments about whether patients have a "right to know", or even a "need to know" about the medications prescribed for them, it is clear that more frequently than not, patients simply have no idea about the medication they are expected to take and even less an idea of why they are to take them. There continues to be an aura about the magic of drugs with the corresponding fear that too much information will dispel their magical powers.

If drug prescribing has developed attributes of irrationality, drug taking may be even more irrational. Consider the following examples:

a) Many patients are advised to take a particular drug before meals, but they take it after meals.

b) Many patients are warned not to use alcohol while they are using some medications, so they give up whiskey and gin but continue to use beer and wine.

c) Some patients are told to take an antibiotic faithfully for ten days, but they stop in three days because the fever is apparently gone.

d) Some patients double the recommended daily dosage, perhaps in the belief that if three pills a day are good, six will be better.

e) Some patients forget to take the medication for three days and then, to recoup, take quadruple the dosage on the fourth day. And

f) Many patients neglect to report an early adverse reaction to their physician or pharmacist and delay until the time comes when costly hospitalization is needed.

It is impossible to know the causes of such irrational behaviour. Part of the blame is directed to physicians who, patients say, give confusing or inadequate instructions, or who offer no instructions at all. On the other hand, physicians complain that these instructions are ignored or misunderstood, or that the patient has been forgetful or uncooperative. There is little question, though, that a substantial problem remains about patient compliance with drug regimes (Sackett and Haynes, 1980).

Who is to blame for patient non-compliance? Obviously the patient must bear some share of the responsibility since it is he who has chosen to be non-compliant. But equally clearly, physicians share responsibility for the problems of non-compliance. The solutions must involve both parties if they are to be successful.

One tool available to provide greater information for patients is the patient package insert (PPI). It is designed to provide patients with information of how the product should be used, possible side effects, contraindications, warnings, precautions, proper method of use, and the possible risks and benefits. Various studies have shown that patients are eager to learn more about drugs and have found the PPIs helpful and informative.

Where the issue of PPIs is heading, and indeed the whole matter of greater public regulation, is difficult to forecast. Except that it seems clear that greater regulation, which is becoming an accepted "fact of life" throughout the world, and as evidenced by such activities as drug utilization review, closed formularies, and other methods of surveillance and review, is increasing at a rapidly escalating pace. It is difficult to foresee a reversal in this activity.

5.4 Regulations

The review of the literature raises a wide range of public policy issues, some of which are illuminated by solid information, but many of which are left unanswered either because of insufficient data or because of conflicting evidence. Among the issues being reviewed are the following: a) use of alternative prescribers (in addition to physicians); b) extent of public benefits (beneficiaries); c) patent protection and compulsory licensing; d) methods of reimbursement to pharmacists (ingredient costs and dispensing fees); e) consumer cost sharing; f) drug utilization review (DUR) systems; 7) formularies; and g) generic substitution.

5.4.1 Use of Alternative Prescribers

The literature deals mainly with the question of the use of pharmacists as prescribers. A summary of the literature has been provided by McGhan and Stimmel (1983) who report on the operation of California Law, AB 717, which permits pharmacists to prescribe and administer drugs under the supervision of a physician. Apart from the experience with pharmacists prescribing activities in the Indian Health Service, very little was known about the ability of pharmacists to prescribe safely and effectively.

The California legislation, which has since been duplicated in Florida, thus offers the opportunity to determine the advantages prescribing authority offers to pharmacy and to the health care system and also what limitations should exist. Additionally, it must also be decided what limitations are necessary to accompany the prescribing authority, what changes should be made in training and certification, what type of physician-pharmacist relationship is advisable, how to answer concerns of conflict of interest if the pharmacist prescriber also is the dispenser, and what drugs the pharmacist may prescribe. The early reports of the pharmacist's activity under the California legislation, however, indicates that pharmacists can prescribe indications appropriately. It is expected that further projects along the same lines will be emerging in other states.

5.4.2 Patent Protection and Compulsory Licensure

The most extensive and thorough study of the issue of patent protection and the effects of legislation requiring compulsory licensure of drug products was conducted by the Eastman Commission of Enquiry on the Pharmaceutical Industry between April 1984 and February 1985. Headed by Professor Harry Eastman of the University of Toronto, the Commission submitted a 510 page report which described and analyzed the functioning of the pharmaceutical industry in Canada and proposed 15 recommendations for further actions.

The Eastman Report (Eastman, 1985), based upon the information contained in 146 briefs to the Commission, 41 presentations by witnesses or groups of witnesses, extensive interviews with experts in the United Kingdom, Belgium, Switzerland, Italy and the Commission of the European Community, as well as from 14 research studies specifically commissioned by Eastman and conducted by Canadian experts, provides the most complete analysis of the Canadian pharmaceutical industry available anywhere. The report is divided into two parts. The first covers the legislative framework governing the production and distribution of drugs in Canada, the history of the Canadian pharmaceutical industry, a market profile of the industry, the structure and behaviour of the Canadian market, and evaluation of the performance (prices and profitability) of the pharmaceutical industry in Canada. The second part deals with policy issues and recommendations and covers such issues as patents and royalties, safety and efficacy issues in relation to authorization for marketing of new products, the retail pharmacy market, the regional distribution of the pharmaceutical industry, pharmaceutical research in Canada, and international trade, transfer prices and tariffs.

The conclusions drawn by the Commission are particularly relevant, both to those who have the responsibility of protecting the public interest as well as to those who pay the cost of prescription drugs, the consumers or the third-party payors, whether public or private. For example, the report points out that the price of the products of "generic drug" firms were 51% of the price of the products of "patent-holding" firms for substitutable products. Thus, the consequence of interchangability and of compulsory licensure is that Canadian consumers and taxpayers paid $211 million less in 1983 than they would have done for the same drugs in the absence of substitution.

The Report also contains an interesting assessment of the effects of compulsory licensing on the profitability of the Canadian pharmaceutical industry. The Report observes that:

> Aggregate data for the pharmaceutical industry in Canada does not show adverse effects from the introduction of compulsory licensing to import in 1969. The overall profitability of firms in the pharmaceutical industry in Canada, measured by their after tax profit on capital employed for the years 1968 to 1982, is more stable than for most industries in Canada and rises in the later years of that period. The profits of the industry are also substantially higher than those for total manufacturing and for most industries.

The 19 specific recommendations of the Eastman Commission are the following:

a) New drugs should be awarded a period of exclusivity from general competition of four years after receiving their Notice of Compliance authorizing marketing.

b) A Pharmaceutical Royalty Fund be established and financed by payments made by firms holding compulsory licences, the payments to be determined by the value of the licensee's sales of compulsorily licensed products in Canada, multiplied by the pharmaceutical industry's world-wide ratio of research and development to sales, as determined by the Commissioner of Patents, plus 4 percent (the 4 percent to reflect the value to compulsory licensees of current promotion expenditures of patent-holding firms).

c) The Pharmaceutical Royalty Fund be distributed periodically to the firms whose patents are compulsorily licensed, each firm's share to be determined by the sales in Canada of its patented products by compulsory licensees multiplied by the firm's ratio of research and development expenditures to total sales of ethical drugs in Canada plus 4 percent (to reflect promotion), all this as a proportion of the same variables for the entire group of firms with patents under compulsory licence in Canada.

d) Conditional on preserving modified provision for compulsory licensing in the Patent Act . . ., limitations on product patents for pharmaceutical products in the Patent Act be removed.

e) Reverse onus for pharmaceutical patents be abolished.

f) Preclinical New Drug submissions should consist of a summary of information of the new drug (certified in Canada by a qualified health professional) and protocol of the proposed clinical studies. Also, approvals for Preclinical New Drug Submissions should be automatic within one month of receipt unless the Health Protection Branch finds reason not to grant them or requires further information from the firm concerned. The approval for the submission should also apply to the protocols for research in Phases 1,2, and 3 which would not require further approval unless by explicit decision of the Health Protection Branch.

g) The Health Protection Branch reorder its activities so as to be able to respond to New Drug Submissions and to Supplementary New Drug Submissions without fail within 120 days.

h) In view of the risk of adverse reactions following the release of new drugs for general distribution to a large number of patients, the Commission recommends that regulations should permit the Health Protection Branch to impose post-market studies on the manufacturer as a condition of permission for marketing.

i) Notices of Compliance be issued without review in Canada for New Drug Submissions and Supplementary New Drug Submissions for pharmaceutical products and medical devices that have not received them in Canada but that have already received Notices of Compliance in the United States and either France or the United Kingdom until the backlog of submissions has been absorbed and procedures reformed to provide clearance delays of no longer than 120 days.

j) An expert committee supported by the staff of the Health Protection Branch be established by statute to make final judgements on the issuance of Notices of Compliance for New Drug Submissions. The Commission also recommends that the various steps in the process of review should make use of statutory advisory committees of outside experts.

k) The Minister of Health and Welfare establish an advisory committee of experts from the Health Protection Branch, universities, hospitals, and industry (thus reflecting the many interests affected) to recommend appropriate regulations and guidelines for the evaluation and clearing of drugs for marketing.

l) No impediment be placed to the access to the use of Product Monographs (which describe the characteristics of new drugs).

m) Measures to take to ensure that pharmaceutical products sold to consumers at retail in Canada should be dispensed in the manufacturer's original package and, further, that complete product information be presented in a way that can be understood by laymen. Indications, administration, dosage, warnings with respect to adverse reactions, a full list of contents, and other relevant information should be included. Provision should be made that physicians could instruct pharmacists to withhold such information from designated patients.

n) All ethical drugs should be prominently labelled with their generic name, whatever other name may appear on the label.

o) Provincial governments should remove all restrictions on the advertising of drug prices, dispensing fees, or the sum of both.

p) Pharmacists should be expressly permitted to provide information on drug prices over the telephone.

q) The prescription receipt should state both the drug cost and the dispensing fee.

r) Provincial governments should ensure that public drug reimbursement programs require a significant contribution to each purchase by the consumer arranged in such a way that price competition is induced, and should encourage private drug insurance plans also to have this element.

s) That government departments should review their procedures for granting financial support to research in the pharmaceutical industry with a view to improving the access of small research-intensive firms to such support by making such procedures simpler, faster, more stable, and more predictable.

5.4.3 Methods of Reimbursement to Pharmacists (see also Section 5.4)

The policy issues involved under this heading include the following:

a) The methods by which pharmacists are compensated for their services. These may include fee-for-service based on ingredient cost and dispensing fee, capitation amounts based on number of eligible beneficiaries, major medical expenditures where the patient pays a deductible and the coinsurance and payment for expanded scope of services.

b) Reimbursement methods for in-hospital pharmaceutical services (including drug utilization) as well as drugs provided to ambulatory patients through community pharmacies.

c) Alternative methods of drug distribution such as mail order, pharmacies in clinics, and Health Maintenance Organizations (HMOs).

Payment for drug benefits has generally followed the traditional fee-for-service service method of payment to the pharmacy, although most pharmacists are employed on a salary basis. The income to the pharmacy, however, reflects the number of services rendered, and thus reflects the incentives embodied in a fee-for-service method of payment. That is, the more services provided, the greater the amount of payment. The fees paid for each service can be made on a variety of bases. One is to pay the pharmacy its "usual and customary" charge for the service rendered. Thus, the charge and the payment varies by individual pharmacy. The second method, which is the more traditional method of payment, is according to an established fee schedule which identifies the fee to be paid for each item of service. A newer method of payment, which combines features of the fee schedule and the "usual and customary" methods, is to compensate the pharmacist on the basis of an established dispensing fee, plus reimbursement for the actual cost of the ingredients contained in the products dispensed. This method of reimbursement for pharmaceutical services was developed in response to the expressed wishes of the pharmacy profession who preferred to be compensated on the basis of a professional fee, in much the same way that physicians are paid for their services.

There are basically two other methods of payment to providers that are alternatives to the fee-for-service system. The first is a straight salary system which is used almost universally in public programs which provide direct services to beneficiaries (such as municipal health programs, school health programs, and the like), and the second is a "capitation" method of payment, used most widely by HMOs.

There have been a wide variety of different systems through which prescription drug benefits have been delivered. The most common way for dispensing non-inpatient drugs is through community pharmacies, both those classified as belonging to a chain as well as independent pharmacies. When prepayment, or insurance, was introduced for the payment of prescription drugs, it was felt that certain conditions or controls needed to be introduced in order to anticipate the cost of providing the benefits and thus enable the establishment of appropriate premiums (see Section 6.2). The conditions were mainly in the form of agreed-upon terms between the third-party payors and those providing the service, the pharmacies in the case of prescription drug benefits. The terms specified the amounts to be paid and the conditions under which they would be paid. This was a legally binding agreement between the third-party payor and those pharmacies that agreed to its terms. These pharmacies thus became 'participating pharmacies' and the subscribers or beneficiaries were assured of the full benefits provided by the program if they utilized participating pharmacies.

There are two other models which have been developed to compete with the community pharmacy method of dispensing drugs. One is based on the so-called 'in-house' pharmacies which are owned, or controlled, by the organization underwriting the drug benefit. Examples of such 'in-house' pharmacies are those operating within hospitals or clinics associated with HMOs and which dispense drugs directly to those enrolled in the HMO.

Another variation on the traditional theme is a scheme whereby prescription drugs are dispensed from a central location and sent by mail to members of the plan or program who are eligible to receive such services. The costs of the mail order drugs are substantially less than those obtained through community pharmacies and are even less than those dispensed in 'in-house' pharmacies. Because of the delays inherent in a mail order program, its benefits are directed mainly to those who have substantial prescription drug costs and to those whose needs are long-term rather than short-term. This applies mainly to people with chronic illnesses rather than those with acute, short-term disabilities. Thus, the groups who are most likely to be attracted to such a mail order drug benefit program are the elderly or the disabled.

5.4.4 Cost Sharing

One suggestion frequently made for controlling or reducing third-party (including public third party) expenditures for health services is to shift part of the cost to patients via the mechanism of patient cost-sharing through payment of deductibles, co-insurance and/or copayment.

While most of the research on the effects of patient payments has been directed at studying its effects on the use of physician services, there have been some studies which have looked specifically at copayments for pharmaceutical services.

Those who have looked specifically at copayment for drug benefits have concluded that the imposition of a copayment for prescription drugs may be an example of being penny-wise and pound-foolish. The study by Roemer et al (1975) at the University of California at Los Angeles, for example, looked at the effects of the imposition of a $1.00 copayment for physician visits and a 50¢ copayment for prescription drugs. They found that while utilization rates for physician services and prescription drugs may have decreased as the result of the patient copayments, hospitalization rates increased. The increased costs of hospitalization more than offset any savings from the reduction of ambulatory service use rates. Higher hospitalization use rates suggest that financial deterrents to the excessive use of ambulatory services such as physician visits and prescription drugs, particularly by poor people, are penny-wise and pound-foolish efforts. This is presumably due to the neglect of earlier medical care because of the inhibiting effects of copayment.

Canadian studies, too, Badgley & Smith (1979); Barer, Evans & Stoddart (1979); and Wolfson and Tuohy (1980) have found that patient charges, if they are sufficiently large to have any effect at all, have a disproportinately negative impact on poorer families and thus a negative consequence on their health status. The use of patient payments, where they are legally allowable, would seem to be inconsistent with the philosophy of equity of access to needed health services under the Canadian national health insurance system.

5.4.5 Generic Substitution

Before the early 1950s, pharmacists were allowed to dispense any labeller's product as long as it matched the active ingredients requested on the physician's prescription. For many years, this practice of drug product selection (substitution) was quite acceptable to pharmacists, physicians, and manufacturers, undoubtedly due in large part to the large percentage of prescriptions which were compounded, and the small proportion of drug preparations that were manufactured in final form.

After World War II, there was a tremendous increase in the development of new and patented drug entities. There also was a decrease in the amount of compounding done in pharmacies and a concomitant increase in prefabricated drug products. Enormous growth occurred in sales of the pharmaceutical industry, especially among manufacturers of proprietary drug products.

This period of growth also marked the beginning of the organized movement against prescription drug substitution by the pharmaceutical industry. It was during the period of the 1950s that effective efforts were made, coordinated largely by the National Pharmaceutical Council in the U.S., to enact legislation prohibiting drug product substitution by pharmacists. So successful were their efforts that by the end of the 1950s, most states in the United States and most provinces in Canada had enacted legislation prohibiting pharmacists from dispensing any product other than the one specifically indicated on the prescription. Soon thereafter, all states and provinces adopted similar "antisubstitution" legislation.

But as rapid as the adoption of this antisubstitution legislation had been, so was the extension of its repeal which came twenty years later. During the period of the 1970s, there was a concerted effort in the U.S. to repeal these antisubstitution laws organized and led by the American Pharmaceutical Association. The first state to repeal the antisubstitution legislation was Michigan in 1974. It was followed in rapid succession by states in all parts of the country and by the end of the decade, over 40 jurisdictions had repealed their state laws. By 1984, all states had abandoned the antisubstitution approach, as had the District of Columbia, Guam and Puerto Rico.

The Canadian provinces were even more active in the repeal of antisubstitution laws campaign. Beginning in 1962, the Canadian provinces repealed the provincial acts to allow drug product substitution (See Eastman, 1985, pp.396-397).

A comprehensive study of the effects of the currently prevailing drug product substitution laws has recently been published by the National Center for Health Services Research and Health Care Technology Assessment of the U.S. Department of Health and Human Services (Goldberg et al, 1986). The monograph, in addition to describing and analyzing the context in which drug substitution laws operate, provides detailed reviews of the research and findings of the various studies which have been conducted in regard to the effects of such laws. This report reviews several hundred studies conducted during the period 1974-1984.

The evaluation of both the scope of our knowledge of various aspects of drug product substitution as well as an assessment of the appropriate degree of confidence that we may place on the findings is presented under ten major topic areas. These are:

a) Consumer, physician, and pharmacist attitudes, awareness and understanding of drug product substitution laws.

b) Changes in the pharmaceutical industry in relationship to drug product substitution laws.

c) Prescription characteristics in relationship to drug product substitution laws.

d) Characteristics of actually substituted prescriptions.

e) Pharmacy and pharmacist characteristics in relationship to drug product substitution.

f) Physician characteristics in relationship to drug product substitution.

g) Method of payment in relationship to drug product substitution.

h) Quality of care in relationship to drug product substitution.

i) Savings from drug product substitution.

j) Provisions of state laws in relationship to drug product subtitution.

The final section of the monograph deals with policy and research implications of our current state of knowledge and the directions for the future. This section highlights needed action in policy and research in four major areas: a) incentives in the pharmaceutical industry; b) enhancing consumer knowledge; c) changing the pattern of physician prescribing behaviour; and d) changing the pattern of pharmacist dispensning behaviour.

5.5 Effects of the Environment on Utilization - The Case of Advertising (see also Section 6.3.3)

Considerable attention has been paid to the question of whether advertising, and particularly print advertising in medical journals, has a major impact on patterns of physician prescribing. A review of the arguments on this issue has been provided by Smith (1983) of the University of Mississippi.

In relating advertising to medical issues, Smith raises the spectre of the possibility that advertising may lead to inappropriate prescribing - either too much, too little, or the wrong drug. His comprehensive review of the literature (Smith (1977); Hornbrook (1978); Walton (1980); and Chapman (1979)) leads to the conclusion that "the weight of published evidence lends little credence to a major effect of journal advertising done on prescribing, for good or ill," although he concedes that the published evidence obviously excludes data from drug manufacturers files which may very well contain evidence to contradict that which has been published.

This review discusses issues of an economic and social nature that are raised in the discussion of advertising. The issues include: a) the amount of money spent on advertising; b) the cost of physicians acting as patient's agents in performing the information search activities; c) the costs of diffusion of drug innovations; and d) the costs of acquiring new knowledge.

Several latent effects of advertising are raised and discussed. The first is the problem associated with the difficulty physicians have in separating the information contained in journal advertising from that contained in other journal content when they cite medical journals as a major source of drug knowledge. Another major criticism is the possible sexist content of the advertising, using the example that many ads excessively use pictures of women as sick or disturbed, and thereby create the image of women as not only the weaker sex, but the sicker sex. Another problem discussed by Smith is the possibility that drug advertising influences not only the promotion of the products themselves, but also influences the process of diagnosing illness.

Smith also reviews the research undertaken by his group at the University of Mississippi. This includes a wide range of issues, including treatment of the following topics: use of humor (namely aimed at physicians or the drugs themselves); treatment of blacks in print advertising; use of sex as the dominant appeal of the ad; treatment of the elderly in a way which reinforces stereotypes of the elderly; and how drug ads deal with problems of anxiety, psychosis and depression.

While defending the advertisers against the attack of those who call for a ban on advertising, Smith concludes by summarizing what we really know about the effects of advertising, which includes the following:

a) A great deal of money is spent on journal advertising.
b) Some indeterminate amount of the money results in: more needed information for prescribers from the journals that are supported by the ads, and some needed information for prescribers from the ads themselves.
c) Someone, the patient or some third party, pays for the cost of the advertising.
d) An objective cost-benefit analysis of the above spending has not been conducted and is probably impossible.
e) The effect of such advertising is more reminder than directly persuasive, but it must play some additional role in the milieu of drug promotion and information.
f) The advertisements sometimes portray patients in ways that are inconsistent with the realities of practice. This may or may not rebound to the benefit of the advertiser.
g) The ads are sometimes deceptive and/or misleading as evidenced by F.D.A. actions.

h) Modest regulatory changes excepted, modifications of the nature and extent of journal advertising must await major philosophical changes concerning the role and scope of pharmaceutical promotion. Such changes, if indeed they are necessary, should be based on rigid, scientific study.

6. INFLUENCES OF SPECIFIC INTERVENTIONS ON DRUG UTILIZATION

6.1 Hospital Restrictions

A large variety of local regulatory and restrictive maneuvers (see Table 3) have been shown to decrease drug cost. Most of the literature supporting these maneuvers is written by pharmacists, therefore the primary goal of cost containment and sound pharmacy practice is not surprising. Virtually all the published literature relating to this describes systems in place in urban hospital settings or hospitals under common governance (e.g. for-profit hospitals). However, such strategies have been complemented successfully in community hospitals and in community medical practice. These measures vary in their effectiveness, acceptability, cost, and ease of implementation.

A prominent weakness among papers describing these maneuvers is the lack of a formal, complete cost analysis of the maneuver. For example, in programs requiring advice or consultation on infectious disease, consultant physician charges are never mentioned. Since some cost savings are so large (e.g. up to 25% of the pharmacy budget) there can be no doubt that there are substantial net savings.

Several features of these maneuvers include:

a) The major assumption of restrictive programs is that quality of patient care is improved or unchanged and that rational decisions about substitution and deletions of drugs can be made from a process of literature review and physician opinion.

b) That they are most easily applied in hospital.

c) Formulary system (see Section 6.5).

d) Clinically trained pharmacy staff.

e) Pharmacy staff provide the leadership and innovation in this area hence require appropriate training.

f) Programs that are targetted on particularly costly/toxic drugs. Targetted drugs include aminoglycosides, cephalosporins, benzodiazepines, parenteral nutrition, prophylactic antibiotics, broad spectrum antibiotics, blood components, H2 antagonists and propoxyphene. Relatively little attention has been paid to psychoactive drugs.

g) The explanation of administrative action and provision of alternative treatment options. Such programs are not primary education since the educational maneuvers are not effective on their own.

h) Multilateral decision-making in support of the Pharmacy and Therapeutic Committee and key administrative individuals (e.g. Chief of Medical Staff).

i) Arbitrary restrictive measures that create considerable ill will. To avoid this an education program is needed as well as an option where all drugs can be obtained under some special procedure. The perceived element of freedom of choice affects attitudes of physicians even if the option requires bureaucracy.

Formulary restrictions or other restrictions, while effective in decreasing use of drugs, may set in motion compensatory changes in prescribing patterns. For example, restricting diazepam may result in an increased use of chlordiazepoxide and oxazepam, and restricting propoxyphene may increase analgesic combinations containing codeine (Shenfield et al, 1980). Of the possible substitution patterns (equal, less or greater efficacy, safety or cost) those of lesser efficacy, or safety and high cost are of special interest.

In some cases the tradeoff is probably pointless from a quality of care point of view; e.g. substituting an equally effective drug with one of identical safety and cost, like diazepam with chlordiazepoxide (Huber, 1982). But more toxic drugs are of particular concern, like codeine (Shenfield et al, 1980) and aminoglycosides (Reilly et al, 1978). In most cases the substitution is a carefully planned one involving careful review to suggest another drug that will be equally efficacious at lower cost with no greater, and occasionally less, toxicity (Katz, 1978 and Craig, 1978) as in cephapirin for cefazolin. The implication of these shifts is that a drug utilization monitoring system must include alternate members of a class in order to detect shifts in usage after a restriction is applied.

TABLE 3: HOSPITAL DRUG RESTRICTIONS OPTIONS

1. COUNTERSIGN REQUIREMENT (e.g.Chief of Staff, Infectious Disease, service P & T)?
2. JUSTIFICATION OF ORDER
3. FORMULARY DELETION
4. FORMULARY REDUCTIONS
5. FORMULARY SUBSTITUTIONS
6. RESTRICTION OF USE TO CERTAIN PHYSICIANS OR SERVICES
7. ADDITION REQUIRES REQUEST FROM CONSULTANT & DOCUMENTATION
8. CONSULTATION REQUIRED (e.g. Infectious disease, pharmacy)
9. LINKED GUIDELINES FOR USAGE - LINKED TO AUDIT
10. END USE AUDIT
11. LIMIT DURATION OF PRESCRIPTION - AUTOMATIC STOP ORDERS
12. RENEWAL ORDERS AT FIXED POINT IN TIME
13. PATIENT CONSENT
14. WEEKLY PATTERNS OF USE REPORTS
15. PHARMACY AND THERAPEUTICS COMMITTEE
16. CONTROL OF LAB REPORTS (e.g. antibiotic sensitivity)
17. REDUCE THERAPEUTICALLY EQUIVALENT PRODUCTS
18. DRUG UTILIZATION REVIEW
19. PHYSICIAN COST CONTAINMENT EDUCATION

6.2 Third-Party Payors

One of the most important influences on drug utilization, both from the impact on amount and pattern of prescribing as well as on patient behaviour, is the type and method by which payment for the drugs is made.

The pattern of payment for prescription drugs has followed a pattern similar to that of other areas of health care costs such as the cost of hospitalization and physicians services. At the earliest stage, such costs were the responsibility of direct payment by the patient or a member of the patient's family. This form of payment is generally known as 'out-of-pocket' payment. At a later period of time, and this was most intensive during the period following World War II, the cost of such services began to be spread over groups of patients, or potential patients, through the device of insurance or prepayment. This generally occurred through arrangements within the private sector such as Blue Cross and Blue Shield. At a still later time, such insurance or prepayment was incorporated into public programs such as the Canadian National Health Insurance program, Medicare and Medicaid in the United States, the National Health Service in Great Britain, and other similar public programs throughout the world.

Thus, while there still continues to be an element of cost (at times very substantial) remaining with the individual patient, there is an increasing portion of the cost which has been assumed by the 'third-party', whether in the form of private or public programs.

The extent of the balance between 'out-of-pocket' payments and payments by third parties depends largely on the type of service considered. In Canada, for example, hospital and medical services costs are largely covered by third-party programs, which fall almost exclusively within the public sector. This is equally true in Great Britain and in many of the European countries, including the communist countries. The United States is the only country which relies heavily on the private sector, with much of the health insurance coverage still being with the private insurance companies or with the not-for-profit plans such as Blue Cross and Blue Shield.

The extent of third-party coverage for drugs is much less extensive than that of either hospitalization or physicians services. Nonetheless, there continues to be a trend toward more people being covered for the cost of prescription drugs, either through public or private programs. Public programs in Canada are directed mainly to the elderly, the indigent or the medically indigent segments of the population. Examples of such public programs are the Drug Benefit Program in Ontario which provides extensive prescription drug benefits to all those who receive social assistance payments or are age 65 or older. Private drug benefit plans also are becoming more popular with prescription drug programs being offered by commercial insurance companies such as London Life, or by non-profit organizations like Blue Cross or Green Shield. The benefits provided to subscribers of these plans, who obtain these benefits usually as a component of employee benefit plans, vary considerably in scope as well as depth of coverage, ranging from fairly broad comprehensive coverage to plans which require substantial deductibles and subscriber co-payments.

The existence and influence of such third-party plans has been recognized by many observers as being a substantial influence not only upon the behaviour of prescribers, dispensers and consumers of prescription drugs, but also upon the costs of drugs which, as presented earlier in this report, have been escalating rapidly. This, of course, also raises the question of how and to what extent these third-parties have incorporated cost-savings or cost-containment into their programs.

A very thorough and penetrating review of the literature on third-party drug benefit plans, particularly as they relate to the issue of cost containment, was undertaken by Knapp and Palumbo. Drs. Knapp and Palumbo are highly regarded as specialists in the area of pharmacy administration and they have gained a reputation of being particularly knowledgeable in the area of third-party plans. Their book, Containing Costs in Third Party Drug Programs, published in 1978, presents an excellent annotated bibliography of books and articles on third party drug programs covering the period from 1970 to 1977. Certain classical articles from the earlier period are also referenced, but most of the material was written during the eight years to which they direct their attention.

The abstracts are categorized into two main subjects which are further subdivided into 12 chapters. The main subject areas and their subdivisions are as follows:

I Cost Containment and Overview
  1. General Aspects of Cost Containment
  2. Controlling Costs in Drug Programs
  3. Experiences in Other Countries
  4. Experiences in Inpatient Settings

II Cost Containment Approaches in Out-patient Drug Programs
  5. Patient Cost Sharing
  6. Direct Provision of Drugs and Pharmacy Services
  7. Drug Cost Controls: Maximum Allowable Cost (MAC) Program
  8. Drug Cost Controls: Product Selection and Substitution Among Multisource Products
  9. Drug Cost Controls: Patent Restrictions, Negotiated Prices
  10. Dispensing Cost Controls: Pharmacist Reimbursement
  11. Prescribing Controls: Drug Use Review
  12. Prescribing Controls: Formulary Restrictions

Of particular relevance to our current review is the fact that Knapp and Palumbo include material related directly to drug insurance programs in Canada, the United Kingdom, Australia, New Zealand, West Germany, Norway, Sweden, France, the Netherlands, Belgium, Italy, and the Soviet Union. Unfortunately, most of the material in this section, as throughout the book, presents summaries rather than critiques of each publication, thus depriving the reader of the thoughtful insights and evaluation of the literature by two very able critics. Equally unfortunate is the fact that the review stops at the year 1977, as much has been written and published since that time.

Fortunately, the American Pharmaceutical Association has published a recent report on third-party prescription drug programs (Abood, 1984). The report prepared by the APhA Pharmacy Commission on Third Party Programs, included a series of working papers prepared by knowledgeable experts and refined by Commission members and review groups of experienced practising pharmacists. The expert consultants commissioned by APhA prepared reports on the following topics:

a) "Legal Issues Pertaining to Third Party Pharmacy Services Programs" by Richard R. Abood;

b) "Structuring Drug Benefits" by Vincent Gardner;

c) "Pharmacy Compensation and Reimbursement" by Stephen W. Schondelmeyer;

d) "Cost Containment" by James W. Richards;

e) "Drug Utilization Review: A Component of Drug Quality Assurance" by Duane M. Kirking;

f) "Forecasting the Future" by William H. Campbell;

g) "Public Relations and Education" by Albert I. Wertheimer and Ronald S. Hadsall.

The commissioned working papers were to include a thorough literature review of any published and unpublished materials pertinent to the assigned third party topics.

Sections of the new report of particular importance in looking at the subject of third party drug benefit plans are the chapters "Structuring Drug Benefits", "Pharmacy Compensation and Reimbursement" and "Cost Containment".

6.2.1 Structuring Drug Benefits

6.2.1.1 Private Programs

This section traces the development of both private and public drug benefit programs, starting with the establishment of the California Pharmacists Association sponsored California Pharmaceutical Services Inc. which was modeled largely on the Windsor, Ontario based Green Shield Plan. This was the first of the prepaid drug benefit programs in the U.S. Services under this plan are generally provided through local pharmacies which contract with the insurance programs and bill the programs directly for the services provided. Program beneficiaries can, however, receive prescriptions from noncontract pharmacies and bill the insurance plan directly. Prescription drug benefits are also provided under most major medical programs. The patient pays the pharmacy for the prescription, submits the claim to the insurance carrier and receives payment from the carrier after meeting any deductible and copayment amount.

Current trends in the financing of health care are changing many of the traditional methods for delivering health care, including prescription drugs. Some employers now offer mail-order services. The development of health maintenance organizations, preferred provider organizations, and other new types of organizations, have influenced both the costs and patterns of delivery of health care services generally, including prescription drugs.

6.2.1.2 Public Programs

Historically, prescription drugs have been covered by a wide variety of public plans for a long period of time. Drugs were supplied through public facilities such as county clinics and hospitals, U.S. Public Service Hospitals and clinics, military hospitals and clinics, and the Veterans Administration.

Since World War II, the U.S. program has extended benefits beyond those provided directly through VA facilities and provided for prescriptions dispensed by community pharmacies. Prescription drug benefits are also provided to beneficiaries of the Office of the Civilian Health and Medical Program of the Uniformed Services (OCHAMPUS). Since 1965 prescription drug benefits have also been provided under the Medicaid program for indigent and medically indigent individuals.

The scope of benefits, methods of underwriting, administration, and payment procedures differ considerably among the various private and public plans. They reflect, however, the diversity of such features in health insurance programs for hospital and physicians' services currently in existence in the United States.

6.2.1.3 New Changes

The review notes a number of new and innovative provisions in both the private and public programs. These include:

a) Drug Utilization Review: It is believed that a good DUR system would produce a positive cost-benefit ratio and would be beneficial for drug benefit plans.

b) Increased Drug Product Selection: Attempts to achieve savings from lower cost, generically equivalent products have utilized two options. The first is the provision of payments limited to a maximum allowable cost (MAC) which has not been incorporated into many of the public and private programs. The second strategy is to use specific incentives to encourage drug product selection, such as variable dispensing fees, sharing of savings, and other similar inducements.

c) Use of Formularies: A consensus is growing that drug formularies have worked well within institutions as a means of controlling drug inventories and costs, and that there should be an attempt to extend this mechanism outside the institutions. Some progress has been made in this direction within HMOs and other organized systems.

d) Group Purchasing: Group buying has been effective in institutional settings. The concept for noninstitutional settings has been under discussion for several years as a possible cost-saving technique. It is difficult to implement, yet several state and local pharmacy organizations have established group purchasing plans as a method for effectively competing for third party business.

e) Therapeutic Interchange: This involves dispensing lower-priced products in place of higher-priced products in the same therapeutic category. While the concept is under study by plan administrators, legal barriers make this option difficult to impose. There is some evidence, however, that therapeutic interchange is now being practised, particularly when there is agreement between physicians and pharmacists on when and what to interchange.

f) Pharmacist Prescribing: Some benefit managers are reviewing the present information available from research studies that allow limited prescribing authority to nonphysician health care practitioners such as pharmacists and nurse practitioners. Many see this option as a viable method for containing overall health care costs by reducing the number of physician visits and by increasing patient compliance with medication directions. Many legal and professional hurdles remain, but it is possible that under well-controlled conditions, some plans, especially HMOs, will experiment with this option in the near future.

6.2.1.4 Comment

Third party drug programs, having matured over the past 20 years, are now undergoing rapid changes that track closely to changes in all areas of health are financing. Pharmacies, if they are to survive these changes, will have to adjust old methods of operation. Change will also be experienced by both pharmaceutical manufacturers and wholesalers. In an effort to deal with health care inflation that has existed for the past 20 years, business firms and government agencies are changing the way third party programs both pay and deliver services (see Section 6.2). New methods of delivery include HMOs, Preferred Provider Organizations (PPOs) and mail-order operations. New methods of payment include capitation rates, global fees, discount rates, and price bids. The lines between providers and insurers of health care are blurring. Pharmacy providers are modifying existing methods of delivering services to meet the changes in the marketplace.

6.2.2 Pharmacy Compensation and Reimbursement (see also Sections 5.4.3 and 6.4)

There are many methods of compensating providers for performing services or for delivering products. These generally fall into one of two basic groupings of payment methods: retrospective or prospective. The retrospective method is usually identified with a fee-for-service method of payment, which has been and remains the most common method of reimbursement of prescription drug benefits as it is for payment of other health care services. However, capitation methods of payment, usually associated with prospective payment systems, seem to be growing in popularity, both for prescription drugs payments as well as other health care services.

A particularly important issue is the effect of payment policies on utilization and costs of prescription drugs. The payment policies of various private and government third party programs have resulted in a number of significant impacts, many of which have been unintended, negative, or both. These include: cost shifting; ineffective control of drug product cost inflation; biases toward certain types of pharmacy providers; and economic incentives to dispense ineffective, unneeded, or inappropriate medications.

Each of these aspects of the process of drug utilization may be important for the topic of drug utilization. However, the last of these issues, dealing with incentives to dispense improperly, is most probably directly related to our study.

The effects of third party prescription drug plans in providing an incentive to prescribe and to dispense may adversely affect drug costs by:

a) resulting in unnecessary, ineffective, or inappropriate medications;

b) resulting in the dispensing of high-cost rather than low-cost generically equivalent products; and c) resulting in the dispensing of prescription medications instead of equally effective, and less costly, nonprescription medications.

6.2.3 Cost-Containment

Issues related to Drug Product Costs include:

a) Encouraging or requiring drug product selection.

b) Providing reimbursement based on a maximum allowable cost (MAC) concept. This has been used extensively in public programs and more recently in some private third party programs.

c) Some third-party programs have attempted to contain costs by limiting reimbursement to the provider's 'actual acquisition cost' (AAC). Under this approach providers are reimbursed for product costs on the basis of the net invoice cost, usually with the provision that the provider need not deduct cash discounts (sometimes limited to some maximum, e.g. 2%) in the determination of AAC. Providers are entitled to be reimbursed at their AAC whether their costs are high or low compared to other providers.

d) An alternative method of payment is on the basis of 'estimated acquisition cost' (EAC) where some third party programs have attempted to contain drug product costs by limiting reimbursement to what is estimated to be a 'reasonable' price at which the product can be purchased. This amount usually is set at a level between the published 'average wholesale price' (AWP) and the lowest cost price for the product.

e) The establishment of a set-formulary. This concept is described and discussed in greater detail elsewhere in this Report. Briefly described, however, the usual formulary limits eligible products, on a therapeutic and/or on a cost basis, to those entities and products approved for inclusion in the formulary. This has proved to be an effective tool for cost containment.

f) Group purchasing has been attempted by a variety of providers who use collective purchasing power to obtain more favourable cost prices. This has proven to result in lower product cost prices for members who are associated with group purchase efforts or by 'bid purchasing' through a limited number of wholesalers.

6.3 Educational Interventions

6.3.1 Pharmacology and Rational Prescribing in Medical Schools (Undergraduate Medical Education)

The teaching of lifelong patterns of information acquisition, decision-making and learning are among the goals of most medical schools. The likelihood that physicians acquire these skills with respect to rational prescribing of drugs is at least partially reflected through the amount and form of pharmacology and therapeutics teaching they receive at medical school. A paucity of pharmacology and therapeutics training has frequently been cited as one of the major factors responsible for poor prescribing habits.

Canadian schools teach less pharmacology than U.S. schools, with means of 75.6 hours and 116.9 hours respectively. Most teaching occurs in year 2 of 4 year programs. Some schools have no formal instruction in pharmacology at all (e.g. McMaster and Southern Illinois), however, it would be incorrect to assume that none is learned. Such schools use a problem based curriculum. In most schools, lectures are the dominant form of teaching (72%), suggesting emphasis on passive learning by students and an emphasis on facts. The GPEP report (General Professional Education of the Physicians for the Twenty-first Century, by the Association of

Americal Medical Colleges, 1984) strongly recommends a major reduction in this form of teaching. Laboratories comprise a very small fraction of teaching and there has been a steady reduction in this over the past ten years. A recent survey of all North American medical schools indicated only 14% had required teaching in Clinical Pharmacology.

In 1980 the Association for Medical School Pharmacology surveyed 110 U.S. medical schools concerning Clinical Pharmacology and 81 or 73.6% responded (Fisher et al, 1980). Of the 81 respondents 36 (44.4%) identified clinical pharmacology as a separate required or elective teaching entity in the third or fourth year of the curriculum. Topics were both specific and general pharmacologic and therapeutic principles.

In 1985 127 U.S. medical schools were surveyed and 88 (69.3%) responded (Nierenberg, 1986). All schools offered a required pharmacology course (96% in year 2). The average number of hours was 114, and at 84% of the schools, a portion of these hours were spent on clinical pharmacology. While only 14% of the schools offered required courses in clinical pharmacology, 87% taught the topic within other required courses. On average 18.4 hours of instruction was given. The distribution by year is 0.4, 10.5, 3.1 and 3.8 hours respectively. Of the 18.4 hours of instruction, 12.0 hours were spent in lectures and 6.3 in conferences or seminars. These required hours were taught by the Departments of Pharmacology (80%), Medicine (7%), and others (14%). The teaching was performed by Ph.D.'s (32%), M.D.'s in pharmacology (36%), M.D.'s in clinical departments (30%), and others (3%). Of the responding schools 60% offered elective courses in clinical pharmacology. The format of these elective courses differed considerably from the required courses: classroom (24%); clinical rotation (46%); and other (30%). The average length of the course was 55 hours or 3.8 weeks. The average number of students taking the course was 22 (of 124 in the graduating class).

Support for teaching these topics was widespread (97%). 87% of the respondents felt that the ideal curriculum should include a required clinical pharmacology course, however only 11% had plans to implement such a course. Opinion with respect to course placement indicated the following preferences: 4th year - 64%; 3rd year - 22%; 2nd year - 1%; and 1st year - 0%. The course format preferences were: classroom - 54%; clinical rotation - 19%; and other - 26% (e.g. combination).

Another interesting aspect of the survey is that in none of the responses was the concept of rational prescribing a focus of instruction; rather, specific topics and treatment of disease categories were considered. Many of these topics (e.g. new drugs and drug monitoring) might be elements of rational prescribing. This suggests that an overall conceptualization of the educational objectives of clinical pharmacology does not exist.

With respect to psychopharmacology and rational prescribing of psychoactive drugs little is specifically known. The University of

Toronto has developed a computer based curriculum database to help in curriculum analysis and planning (Buckenham et al, 1986). The content of each medical curriculum teaching unit (e.g. lecture, seminar, or lab) of nonhospital based teaching in the first three years is coded with five keyword phrases plus codes for department, teaching format, etc. The data are stored on an IBM-XT (20 mB hard disc) using Knowledgeman II software (Microsoft Systems Inc.). This application software permits identification of overlap and correlation. For example, redundancy with respect to pharmacologic teaching about compliance (5 hours), receptors (10 hours) and drug abuse (10 hours) is easily identified. Similarly, therapeutics is identified as a major omission.

In the four year curriculum at the University of Toronto, psychopharmacology key wordphrases occur in 78 curriculum hours (total keyword hours for all psychiatry content is 146 and pharmacologic content is 273). Of the psychiatric or pharmacologic content in a curriculum only 61% and 51% respectively are taught in the nominal course by that title, i.e. Psychiatry or Pharmacology. Psychopharmacology content occurs in pharmacology (50%), psychiatry (11.5%) and physiology and neuroscience (65%). Prominent overlap areas are alcohol (19 hours), depression (10 hours), and receptors (12 hours). Only 7.7 hours concern therapeutics and the dominant teaching format is lectures (63%). These data indicate that only 18.6% of all pharmacology and psychiatry content of a curriculum concerns psychopharmacology content. This seems small relative to the extent of drug use. Much of the teaching occurs outside traditional departmental jurisdictions where didactic teaching dominates (Romach et al, 1986).

Also, at the University of Toronto there is a required 20 hour course in year 3 as part of a total of 147 hours of Department of Pharmacology teaching and 247 hours of structured pharmacologic content in the total undergraduate program. Nevertheless, relative to other therapeutics teaching (e.g. surgery) little emphasis is placed on rational therapeutics in any medical curricula.

Several problems are apparent with respect to undergraduate medical education and pharmacology, including:

a) lack of vertical and horizontal integration - pharmacologic teaching is scattered across all years and subjects;

b) excessive emphasis on lectures;

c) lack of structures and problem-based opportunities for students to acquire and practise the problem solving, decision-making and integration which will characterize their post-graduate lives;

d) lack of structured active learning;

e) lack of early clinical exposure to clinical problems in the context of basic science to permit application and generalization; and

f) lack of innovation in medical education in pharmacology (only seven innovative teaching programs have been identified in North America).

Strategies consistent with the GPEP report recommendations and which can be considered a remedy to these problems are:

a) making the organization unit for planning and implementing pharmacology teaching multidepartmental in nature;

b) reduction of lecture time 1/2 to 1/3 in many schools;

c) introduction of substantial problem based case study components in the curriculum with a net increase in pharmacologic therapeutic content hours;

d) involvement of students in real clinical situations early in medical school and use real patients as a basis for case studies;

e) monitoring of these changes with objective curriculum content analysis (Buckenham et al, 1986); and

f) development of innovation and evaluation projects around these initiatives.

These or similar initiatives are needed. Given the frequency with which drugs are used by physicians, is it reasonable to expect that 75 hours of formalized teaching in pharmacology, plus a variety of largely chance encounters with drugs in use, can provide a basis from which the skills for optimal prescribing can be developed?

6.3.2 Continuing Medical Education (CME)

It is beyond the scope of this review to consider the efficacy of all continuing education in modifying physician behaviours or patient outcomes. However, such literature is clearly pertinent since pharmacotherapy represents but one type of treatment maneuver in a context requiring accurate diagnosis, sensible decision-making and monitoring of patient outcome. Haynes et al (1984) concluded that "practitioner behavior can be improved by CME interventions". They observed that the likelihood of such an impact was dependent on the intensity of the maneuver. Simple measures such as self-study packages and incomplete feedback (e.g. posted criteria on charts) had inconsistent effects. More complex strategies result in more consistent and sustained effects. Over 240 papers concerning the efficacy of education on prescribing were reviewed, and predetermined standards to assess their quality were applied (Sellers, 1986). Of the 240 papers only two (Avorn et al, 1983 and Schaffner et al, 1983) met the methodologic standards to permit conclusions. The standards used were:

a) design - randomized allocation of physicians or functional units of physicians to intervention and control groups;

b) intervention - replicable description of an educational or administrative intervention intended to improve physician performance or patient outcome;

c) subjects - definition of target experimental group;

d) outcome - assessment of the intervention in terms of learner satisfaction, knowledge gained, behaviour change, and skill acquired in terms of objective change in physician knowledge, skills or behaviour or patient outcome;

e) data analysis - provision of sufficient data to determine delineation of the statistical, clinical and educational importance and assessment of at least 80% of study participants; and

f) trial size - sufficient power in the study.

Unfortunately most of the reputedly best literature in this field are non randomized control trials with post hoc control groups or control groups clearly not comparable with the intervention groups in the pre intervention period, or in which no attempt was made to determine or ensure comparability of the control group. Some studies clearly demonstrate major control group effects indicating that that environment and not the maneuver was responsible for the effect.

A variety of methodologic (design, execution, and analysis) weaknesses in this literature can be summarized as follows:

a) All studies use one form or another of practice audit to measure the results of the intervention rather than actual practitioner behaviours and patient outcomes. In this case the indicator condition for quality of care is a drug and its appropriate use (Chambers et al, 1981). In most cases little care is given in developing the criteria for the indicator condition, its scoring, its pretesting, revision, reliability and validity testing.

b) Most studies fail to blind the auditors to the group, intervention or control, that the physicians were in.

c) Intervention outcomes are uniformly defined in terms of statistical differences, not clinically important change.

d) The trials are of too limited a size to permit answering the putative question(s) of interest.

e) The description of the setting, target physicians, maneuver, and patient population is extremely sparse, suggesting that these factors were not viewed as being of critical importance.

f) There is often insufficient data for statistical analysis, and the impression often gained is that much of what is going on is missed.

g) With respect to follow-up there is less than 80% assessment of outcomes for participants.

h) Open retrospective control designs are used rather than designs incorporating random allocation and concurrent controls. This latter point seems particularly important to distinguish an education intervention from non-specific effects.

i) Cost of the education intervention is rarely determined, while the audited cost saving of the intervention is frequently calculated. In turn,. the impact of the educational maneuver on patient health outcome is not determined. In view of the cost of effective educational maneuvers, cost-effectiveness studies of alternative maneuvers are needed.

Educational interventions have generally focussed on antibiotics and specifically on cephalexin, chloramphenicol, clindamycin, tetracyclines, oral :ephalosporins, antibiotics for urinary tract infections, gentamicin, cefazolin, vasodilators, propoxyphene, cimetidine, antipsychotic drugs, ASA-acetaminophen-codeine combinations and older drugs. Presumably, antibiotics are frequently chosen because of the relative precision of clinical indications, diagnostic testing, ease of detecting side effects, existence of treatment guidelines, cost and frequency of use. These features assist in audit by non-clinical staff. The lack of studies involving psychoactive drugs, considering their extent of use and concern with toxicity, is surprising.

No evidence exists to suggest that general drug information bulletins, as frequently distributed in community hospitals, modify prescribing practice (Fendler et al, 1984). In addition specific programs that focus on a perceived problem area such as education handouts (Berbatis et al, 1982) and specific unadvertisments are without effect (Avorn and Soumerai, 1983). House staff knowledge about drug prices is not increased by a price guide (Babington et al, 1983); and while a single session video instruction program increases physician knowledge it does not alter drug utilization (Neu and Howrey, 1975).

Avorn and Soumerai (1983) reported that six mailings of specially prepared unadvertisments plus two office visits for feedback on specific drugs (vasodilators, cephalexin, propoxyphene) and discussion decreased Medicaid prescribing 14% for the target drugs, decreasing the cost per MD by $105/9 months. They concluded that the savings exceeded the cost of the intervention.

Schaffner et al (1983) showed that office visits of a physician concerning target antibiotic drugs decreased the number of prescriptions (54%) and the number of patients receiving them (44%), whereas a drug educator and educational brochure had no effect. The intervention in this study was nominally brief (15 minutes) and was confounded by its sponsorship by the State Medical Association.

In addition to modifying the use of targetted drug(s), interventions may have other effects. For example, one study in a community hospital showed an increase in valid indications for use of the targetted drugs. However, there were also significant increases in microbiologic testing, measurement of drug levels and use of less toxic drugs (Gilbert et al, 1978). Similarly, in another study a decrease in propoxyphene use was accompanied by a temporary increase in ASA-acetaminophen (Berbatis, 1982).

Although the majority of these studies outcomes seem positive, the effects are generally transient. Exceptions to this generalization have been seen when focussed feedback is provided after the educational intervention. In these cases the duration of effects can be increased up to 9 months (Avorn and Soumerai, 1983) or even 2 years (Ray et al, 1985).

Interventions based on real prescribing by specific physicians seem to be effective. For example, prescribing decreased: a) in a study coupling a list of drugs prescribed with a discussion with a physician colleague (Harris et al, 1984); b) when physicians were asked to justify their presriptions to an infectious disease specialist (McGowan and Finland, 1974); and c) when warnings were given to physicians prescribing large amounts of addictive drugs. These effective strategies share elements of audit, scrutiny and specific feedback about a particular prescribing pattern.

The most appropriate prescribers seem to be younger, more recent graduates with additional courses or postgraduate training, who maintain large, busy practices with more ancillary assistants and who spend less time with patients. They are more cosmopolitan, modern, concerned with psychosocial and quality dimensions of medical care, and tend to practise in a group. They consult and refer their patients frequently and rely more heavily on journal articles for new drug information. Good prescribers are more satisfied with prior training in therapeutics. Finally, the better prescriber is critical of the pharmaceutical industry and supports an expanded role for the (Federal) government in regulating drug quality and costs.

Appropriate prescribing is unrelated to the following: a) physician years of postgraduate training; b) conservative/liberal orientation; c) attitude toward prevention; d) perception of ADR as a problem; and e) patient socio-economic status (Stolley et al, 1972). The absolute number of prescriptions written per patient varies with years of post-graduate training. Residents in family practice training prescribe fewer drugs than faculty members, first year residents prescribe the fewest and third year residents the most (Jackson et al, 1985). With respect to who pays, prescription rates are lowest for self-pay, highest for third party insured and intermediate for Medicaid. Generally, studies concerning interventions are of low methodologic standard with some exceptions (Avorn and Soumerai, 1983 and Schaffner et al, 1983). From these studies and complementary fragments discerned from other studies, sustainable effects on drug prescribing can be achieved by designing interventions that:

a) are based on real patterns of prescription by individual physicians in the practice environment, thus requiring some type of audit process to be in place;

b) target users/heavy prescribers;

c) focus on specific drugs associated with problems of improving quality of care (e.g. antibiotics);

d) make use of special educational materials for the intervention (e.g. unadvertising employing behavioural principles);

e) incorporate individual feedback on drug pattern, and identify possible problem areas; and

f) include individual verbal counselling or meetings about drug use.

Conversely, sustainable effects on drug prescribing are not achieved by: drug bulletins, public awareness campaigns, lectures, seminars, videos, cassette audio tapes, price lists, reminder notes or checklists, decision-making algorithms, handbooks, guidelines, focussing on cost as an issue, mailed brochures and "unadvertising" alone.

The literature concerning modification of drug prescribing behaviour has not addressed the following questions:

a) Do interventions work better on poor prescribers?

b) Can repeating the intervention with non responders at a reasonable interval (e.g. 3 months) improve impact?

c) Do interventions that modify the prescribing of one type of drug generalize to the prescribing of other types of drugs?

d) What is the minimal audit, intervention and feedback package?

e) What are the subspecialist category responses?

f) Is there a differentiation of postgraduate trainee from practicing physician?

g) is there differentiation between foreign medical graduates and Canadian graduates?

h) are any of the interventions cost-effective? and

i) are there differences in the effectiveness of educational maneuvers in teaching hospitals and non-teaching hospitals?

6.3.3 Advertising (see also Section 5.5.)

A great many studies on how doctors learn about drugs have been conducted. However, different physician samples have been used and different questions asked, hence the results are not fully comparable. Some studies focus on attitudes about advertising versus the usefulness of the information and its accuracy. Other studies fail to distinguish between influences on awareness and on prescribing; between information about new drugs vs. existing products; or between commercial vs. non commercial sources of information (Bauer et al, 1966).

Much commentary about drug advertising takes a position of either discrediting or criticizing pharmaceutical companies or defending such advertising. Attempting to avoid this we take a utilitarian point of view. That is, how do physicians become aware of drugs? Do they use drug advertisements and if they do, do they find them useful and how are they used?

With respect to new drugs, commercial sources of information (e.g. detail men - 68%, medical journal advertisements - 32%, and direct mail - 25%) are more useful than non-commercial sources (e.g. journal papers and articles - 40%, MD conventions - 24%, and staff meetings and conventions - 16%) (Gaffin et al, 1959). Physicians first hear of new drugs through commercial sources (detail men - 37.7% and direct mail - 19.2%) but not to the exclusion of the other sources. The picture that emerges is that awareness about new drugs sometimes comes from commercial sources, and that purely scientific sources do not necessarily induce awareness.

Considerable evidence, much of it more than 20 years old, indicates that physicians exercise considerable discretion and variation in where they get information about how to prescribe. Sources of variation are the physician, the drug, the seriousness or complexity of the disease, and acute vs. chronic illness. Physician source preferences may relate to the physician's role. If he/she is consulted about drug therapy and needs to be fully informed, noncommercial sources tend to be used. Professional sources of information dominate as illness severity and complexity increase. Conversely, when the diagnosis is not critical, when trial and error is common or the illness rather trivial, commercial sources of information are more commonly used. From a communications theory point of view, physicians have a multiplicity of information sources and they exercise selectivity with respect to which source they will pay attention to; e.g. some may be discarded for a while and be brought back into play when needed. What is left unaddressed, however, is to what extent poor prescribers rely on drug ads more than good prescribers? Unfortunately no study to address this has been conducted.

Detailed analysis of drug advertisements clearly establishes that they do not serve an educational role but an informational one (Ingelfinger, 1972). Their style, emphasis, and frequent factual errors of commission and omission and education principles precludes any other conclusion. Even if all the facts were correct this would not make advertisements educational since education about use is the issue, not its dispassionate pharmacology or therapeutics.

Similar conclusions can be drawn about detailing. The literature is relatively helpful on ways to refine the above strategy, which include:

a) targeting the intervention on prescribers who do not meet initial reference criteria for indicator condition; b) follow-up of indicator condition 3-6 months post intervention and repeat the same intervention or another in a non-responder group; and c) repeating the process on a non-responder group.

6.3.4 The Pharmacist

The pharmacist fills a valuable resource role in counselling both physicians and patients. In the 'counselling' role the pharmacist is in a key position to increase rational drug prescribing. Pharmacists as direct educators of physicians was shown to be an effective intervention (Avorn and Soumerai, 1983) and the success of this group in the role of 'clinical pharmacist' has been well documented (Lee, 1979). (See Section 5.2.1) Pharmacists also have potential influence in their role as patient counsellors. It has been suggested that pharmacists are not realizing their full potential to influence prescribing behaviour (Knapp et al, 1978). It would seem therefore, that role-specific pharmacist education could increase this influence and prove to be a valuable intervention strategy aimed at achieving rational drug use.

6.3.5 The Patient

Education directed at the patient by pharmacists takes different approaches, primarily verbal or written. Verbal communication occurs at the time of dispensing medication and attempts to increase compliance of drug taking by providing information about the correct and intelligent use of the drug. This form of dissemination has become known as patient counselling and is increasingly used as part of the dispensing process.

Written information has the same goal, but provides the added advantage of accompanying the medication and thus being referred to in multiple instances. Mechanisms such as Patient Package Inserts (PPI), Supplemental Information on Medication (SIMS), Prescription Advisory Leaflets (PAL), and auxilliary labels of an informative or cautionary nature are all examples used in practice. Research has demonstrated that effective education of the patient occurs through a combination of verbal communication and written information.

Consumer groups and the lay press have attempted to inform consumers about the cost advantages of using generic drugs. It appears that a greater degree of success is achieved when the consumer is responsible for his own drug costs, and not when he receives drugs as a benefit of an insurance program.

6.4 Payment Mechanisms for Pharmacy Services (see also Section 5.4.3)

Traditionally, pharmacists have had a dilemma in assessing charges for their services. This continues to be the case because both a product and a service are provided simultaneously. Until recently, pharmacists have not been able to separate these components for purposes of assigning costs to each.

Historically, pharmacists have been merchants (providing a product) and professionals (providing a service). Costs were recovered by charging a markup based on the cost of the product. If the markup was sufficient, it recovered the costs of overhead and service (labour), and provided a profit. This method of pricing, however, does nothing to separate the merchant role from the professional role. In addition, with this method of pricing comes the need for different markups depending upon whether an inexpensive or costly drug is prescribed. Caution must be exercised in order that pharmacists are not perceived as price gougers. Another disadvantage encountered is when less than a full stock container of medication is prescribed. The markup system provides for cost recovery of the amount of product sold. The balance remains in inventory and incurs a carrying cost until it is sold.

One approach to separate the commercial role from the professional role of the pharmacist was the introduction of a suggested schedule of fees. This schedule called for an ingredient cost plus a fee for providing the product to the customer. There was no systematic way of calculating the fee other than its amount relative to the cost of the ingredients and an estimation of time required to dispense the medication. These fees had to be sufficiently high in order to cover overhead and labour costs and, at the same time, provide a reasonable profit. Thus, some schedules suggested sliding fees that escalated with product costs and others suggested flat fees to be added in all cases.

It was not until the late fifties that further progress was made in separating the two roles performed by pharmacists and charging separately for the product and the service. Costs of dispensing were identified and quantified. The tasks of each pharmacist were the same, however, the costs incurred were individualized because of the different overheads of different pharmacies.

The major costs of dispensing drugs are categorized into four areas: a) labour and containers (direct costs); b) overhead of the pharmacy department (indirect costs); c) return on investment in prescription inventory (opportunity costs); and d) general and administrative costs of operating the pharmacy department (management costs). When summed and amortized over all prescriptions dispensed, the resultant cost represents the average cost of dispensing. This is added to the cost of ingredients to arrive at a prescription charge. This model assumes that, on average, the time, service, responsibility, and liability for dispensing each prescription is equal. Therefore the charge assessed should be equal in each case. The only variable is the product cost in each prescription. Thus, the commercial role is separated from the professional role and fees are not a function of product cost.

Since a pharmacist's revenue is tied to the dispensing function, there is no incentive not to dispense a product. As with the fee for service concept, revenue is a function of services performed. In order to separate the two roles further, the suggestion of capitation fees has been proposed. With capitation fees, payment is assessed on a per capita basis for a given population and paid to the pharmacist periodically. The implied assumption is that a greater number of 'healthy' or non-prescription taking clients can be cared for than prescription taking clients. The incentive to earn greater revenue is tied to caring for larger numbers of 'healthy' clients. The trade off in costs is between a flat fee per client, and the cost of medication required by a less healthy population.

While this approach to prescription charging satisfies a separation of roles, it is dependent upon accurate cost forecasting, sufficient clients, and the health status of a defined population. This method attempts to control drug costs by disassociating a pharmacist's revenue from the number of prescriptions dispensed. The concept has been tried in pilot programs, however it has not been widely accepted by pharmacists.

6.5 The Effect of Hospital Formularies on Drug Utilization

The formulary system is a method whereby the medical staff of an institution, working through the Pharmacy and Therapeutics Committee, evaluates, appraises and selects, from among the numerous available drug entities and products, those considered most useful in patient care for a specific setting (ASHP, 1978).

The major product of the formulary system is the Hospital Formulary (Dinel et al, 1972) which is a continually revised compilation of pharmaceuticals that reflects the current clinical judgement of the medical staff. Hence, it is not a simple listing of drugs available at the pharmacy (Dinel et al, 1972 and ASHP, 1978).

The potential benefits of a formulary are three-fold: (a) rational drug therapy; (b) cost control; and (c) education (Hoffman, 1984). Although the potential benefits of a formulary have long been noticed, the question remains as to how effective formularies have been in attaining these goals.

6.5.1 Formularies and Rational Drug Therapy

The formulary is intended to improve the quality of drug therapy by restricting the prescribing choices to pharmaceutical preparations whose relative safety and efficacy have been judged superior to competing agents. Several studies have shown that the inclusion or deletion of a particular drug into the Hospital Formulary is a major determinant of the use of drugs in a hospital (Hoffman, 1984 and Abramowitz, 1984). For example, the removal of propoxyphene HCl from the formulary of a teaching hospital reduced its use from 40% to less than 1% (Hoffman, 1984). Similar findings have been reported for other drugs (Huber et al, 1982 and Anandan, 1981). However, a major study of formularies in 52 teaching hospitals in the USA found that the proportion of drugs, whose relative safety and efficacy were not up to s ndards, included in the formularies ranged from 9.3 to 69.7% (cker and Visconti, 1978). Lack of skills in comparative pharmacc ogy and th rapeutics on the part of physicians and pharmacists and e lack of feed-back from drug utilization studies are given as r jor reasons for the inclusion of drugs into formularies that do ot meet scientific requirements of efficacy and safety (Rucker an Visconti, 1979).

The inclusion or deletion of a drug from formulary must be taken in the context of all other drugs incluc d in the formulary. For example, gentamicin use increased aft r the deletion of cephalosporin in a hospital formulary (Reilly al, 1978). Shifts in prescribing toward potentially more toxic an expensive drugs may result from an isolated restrictive measure (Pl ridge et al, 1984). In summary, limiting drugs through a formulary ay influence which drugs are given, but will not necessarily lea to a more rational approach to therapy (Harding et al, 1985).

6.5.2 Formularies and Cost Control

The Hospital Formulary is "the founda on of any system to contain drug costs" (Abramowitz, 1984). Mos studies have been directed at controlling antimicrobial use since hese drugs account for 19% of total drug budget (Rucker, 1982). veral studies have reported savings ranging from 25-55% using vari techniques (Craig et al, 1978 and Kunin et al, 1973). These stuc s, however, do not appropriately address the impact of deleting he antibiotic from the formulary on actual patient care. For example, no study included patient outcome or other measures of improving rational drug therapy (Craig et al, 1978). In addition, cost-effectiveness studies concerning restrictive formularies found that while drug costs fell, other related costs rose (Hefner, 1979). Therefore, control of the costs of drug use by deleting formulary drugs should be implemented carefully, with an awareness of its potential consequences on patient care. It should be viewed as only one way in which drug costs could be controlled (Hoffman, 1984 and Plumridge et al, 1984).

6.5.3 Educational Aspects

User acceptance is essential for the implementation of a formulary (Hoffman, 1984; Plumridge et al, 1984; and Harding et al, 1985). Change is more likely achieved when there is continual and active participation from users and when information accompanies the guidelines or formulary (Harding et al, 1985). Simple communication of guidelines has little impact and has resulted in the inappropriate use of the formulary (Plumridge et al, 1984). In contrast, lectures, personal contact, individualized feedback and written material promoting formulary use have been found to be more effective on changing drug use patterns (Check, 1980). This suggests that communication should be personalized rather than dictatorial (Lamay et al, 1981).

The goal of hospital formularies is to improve the quality of drug therapy and, hence, patient care. While some studies achieve this goal (Hoffman, 1984; May et al, 1974; and Huber et al, 1982), others fail due to inadequate preparation and implementation (Rucker and Visconti, 1978 and Plumridge et al, 1984). However, with the implementation of the DUR program and other measures of quality assurance, hospital formularies are more likely to achieve their goals.

6.6 DUR/Post-Marketing Surveillance

Stolar (1978) defined a DUR program as an authorized, structured, ongoing system for improving the quality of drug use within a health care organization, which is to be evaluated by using predetermined standards. The object of a DUR program is to correct patterns of drug use which are not consistent with these standards. It must also include a mechanism for measuring the effectiveness of these corrective actions.

Wardell (1978) argues that the increasing number of national and international studies of drug utilization implies that some attention will be given to the results of such studies. Under many medical and regulatory systems, this means that some form of control will be exerted or attempted. He indicates that many programs already exist to control the utilization of therapeutic drugs.

Wardell examines the purpose, mechanisms, achievements and implications of drug utilization control programs. He concludes that most utilization-control systems were implemented for the purpose of constraining drug costs under third-party schemes. In some countries these control systems have easy access to large computerized data bases that exist for purposes of reimbursement and accounting. Typically, these data bases have information on each prescription, identifying the kind and amount of drug used, the prescribing physician, and the dispensing pharmacy. In addition, some systems have information on the patient's identity and the medical reason for which the drug was prescribed. These systems are readily adaptable to setting up and enforcing elaborate utilization controls. Criteria can be set for the identity and quantity of the drug, the condition for which it is prescribed, the type of physician or pharmacist, and the patient, or any combination of these. Failure to meet all the criteria can be made grounds for rejecting reimbursement of the prescription costs by the third party payor. These systems thus have the potential to control the way in which costs of drugs are reimbursed.

For sound public policy decisions regarding utilization controls Wardell suggests the following:

a) The goal(s) of any proposed utilization control system or any particular aspect of the system should be clearly defined. In order to determine whether the stated goals are actually being achieved formal evaluation should be part of the design and implementation of the system. In particular, the evaluation should try to detect and measure any undesired effect.

b) For any system designed to constrain drug costs, the evaluation should, at minimum, measure the total amount actually saved on drugs and compare this with the total cost of setting up, implementing, and administering the cost-constraint system.

c) Formal and more extensive cost-benefit analyses should be undertaken to assess the total medical impact of utilization control systems as measured by rates of mortality and morbidity, gain or loss of earnings, and comparative total costs of all forms of treatment for the disease in question. Detailed attention should be given to the effects of utilization controls (particularly cost constraints) on the expected rate of return from research and on the discovery and development of drugs and medical devices in the future.

d) To improve utilization, alternatives to regulation need careful consideration. Continuing education of physicians and patients is one realistic alternative. However, a clear distinction must be made between education aimed at cost constraints and education aimed at improving the quality of prescribing.

The issue of whether or not post-marketing surveillance (PMS) can help to effect optimal drug therapy is discussed by Strom and Melmon (1979). PMS assesses the epidemiology of drug use and monitors beneficial or harmful effects of drugs following marketing. Strom and Melmon argue that, if used systematically, PMS can substantially improve drug therapy in the United States. This can be accomplished by generating information on drug use and effects (otherwise unavailable), by enabling a more efficient drug approval process, and by educating drug prescribers. However, to be successful, Strom and Melmon feel that PMS will need a good deal of input from prescribers.

In the United States the most effective PMS systems are: a) voluntary reporting to the FDA, drug companies, and medical and pharmacological journals; b) research oriented systems, like the Boston Collaborative Drug Surveillance Program, the Boston University Medical Centres Drug Epidemiology Unit and the University of Florida - Shands Teaching Hospital Drug Monitoring program; and c) some "phase 4" studies of selected new drugs by pharmaceutical manufacturers. Such studies were mandated by the FDA as a condition for the marketing of cimetidine and prazosin.

The authors comment that the most effective overall effort at PMS is the United Kingdom's "yellow card" system of voluntary reporting. In this system when a physician suspects a drug reaction, he submits a brief case report on a business reply card that is folded and mailed directly to representatives of the Committee on Safety of Medicines (CSM). The CSM compiles the results of its surveillance and reports them by means of scholarly publications in medical journals, pamphlets, and "alerts". Reports to the CMS have included oral contraceptives and thromboembolism, chloramphenicol and blood dyscrasias, antiarthritic drugs and blood dyscrasias, liver damage and peptic ulceration, monoamineoxidase (MOA) inhibitors and hypertension, and aerosol bronchodilaters with sudden death. Unanticipated effects of approved drugs are also documented. These include adverse effects (e.g. hepatitis with isoniazid) and positive effects (e.g. the antiarrhythmic and antihypertensive actions of propranolol).

7. FINDINGS IN SPECIAL POPULATIONS

7.1 The Elderly

With respect to drug use, the elderly are a population of special interest (WHO Report, 1981). They comprise an increasing proportion of the population (9%) and account for 28% of the total drug consumption. Frequently they receive more than one drug. For example, data show that the elderly in the community receive an average of 3.2 drugs (Canadian data); those in long term care facilities receive 8.0 drugs (U.S. data); and those in acute care hospitals receive 4.6 drugs (Scottish data) (Lawson et al, 1976).

Typically the elderly are cared for by older physicians. These less recent graduates tend to have poorer drug prescribing habits and generally offer poorer quality of care. In addition, institutionalized patients often receive their medical care from a dominant physician responsible for the entire institution. This restriction in the number of physicians involved restricts opportunities for the scrutinization and discussion among colleagues.

Of particular concern is the high rate of acute and chronic prescribing of psychoactive drugs to institutionalized and ambulatory elderly patients. As many as 43% of elderly patients in 173 Tennessee nursing homes receive an antipsychotic drug - 9% of these chronically (Ray et al, 1980). This study shows that physicians with large nursing home practices prescribed 81% of the total antipsychotic medications. Moreover, as nursing home practice size increased, so did the number of drugs prescribed per patient.

Drug absorption, metabolism, and effects are often altered in the elderly (Greenblatt et al, 1982). With respect to the risk of anticholinergic toxicity, Blazer et al (1983) found that 21-32% of nursing home residents received two or more such drugs, while a comparable ambulatory group received 11-13%, and 41 out of 3462 patients received 5 or more at one time. This study reveals that physicians did not choose drugs selectively in order to minimize the potential for anticholinergic toxicity, and suggests that the risk of anticholinergic toxicity may be under estimated by physicians.

Several studies indicate large numbers of p.r.n. orders (Ingran et al, 1975 and Segal et al, 1979) and the possible misuse of drugs in the elderly (Ray et al, 1980; Blazer et al, 1983; and Stults, 1982). For example, epidemiologic evidence suggests the misuse of antipsychotic drugs (Ray et al, 1980). Concern over the use of digoxin in the elderly (Stults, 1982) is increasing. In many instances its use may not be clinically justified. Given the high utilization rates, age-related alterations in pharmacokinetics and other poorly understood risk factors, the frequency of digoxin toxicity in the elderly is considerable.

Several conclusions concerning drug use among the elderly can be reached including:

a) Considerable evidence exists for drug overuse and misuse in chronically institutionalized elderly patients.

Systematically developed multi-institutional pharmacy service strategies, drug use guidelines, and audit and education programs for MD's and nurses would have considerable impact.

b) Targetting of restrictive/educational maneuvers on high risk, high cost drugs and individual physicians is possible, particularly in institutional settings.

c) Comparisons among institutions would identify deviant patterns of use, thereby providing a basis for targeting decisions.

d) Large group practices provide community based setting for drug use audits.

e) Linkage of drug use patient demographics and diagnosis is essential in the elderly.

f) To a greater extent, the elderly self medicate with analgesics, vitamins, and laxatives.

g) Aging per se does not alter compliance, however memory, visual impairment and a decrease in the access to ready help can all impair the quality of patient care. The consequences of poor communication and understanding can be more serious with the elderly than with a younger population.

h) All drugs have the potential for harm. However age and number of drugs used are associated with higher adverse drug reaction (ADR) rates (Hurwitz, 1969). The elderly, therefore, are at special risk. Up to 20% of geriatric patient hospitalizations are ascribable to ADR or errors in drug dosage.

Strategies are available which can effectively modify drug utilization. The principles of pharmacotherapy in the elderly are identical to other patient populations. In hospital settings a combination of restrictive and educational intervention strategies have proven to be effective modifiers of drug utilization. For instance, a laxative utilization review program was conducted at a large long-term care hospital (Elzarian, 1979). The problem areas of utilization were identified, followed by an intervention period which utilized various educational methods targetted to physicians and nurses. There was a decrease in mineral-oil prescribing and an overall decrease in laxative use and in laxative costs.

7.2 The Poor

The population of Tennessee in July 1974 was estimated at 4,129,000. During July 1974, 317,943 persons were eligible to receive Medicaid benefits and there were 102,611 recipients for whom claims were paid (Ray et al, 1976). During this month the Medicaid program paid for 200,893 prescriptions for legend drugs, including 16,896 prescriptions for antibiotics. Antibiotics were the third ranking class of drugs (after cardiovascular-antihypertensive drugs and tranquilizers) and accounted for 8.4% of all legend drug claims.

The age, sex and race distributions of the ambulatory patients receiving chloramphenicol prescriptions reflected the composition of the Medicaid population. 82% were 18 or older, 71% were women, and 79% were white. The distribution of patients by the number of prescriptions written was strikingly skewed. Although 65% of the ambulatory chloramphenicol recipients obtained only one prescription, seven persons obtained ten or more. A few patients were exposed to large amount of chloramphenicol; indeed two adults received more than 250 grams.

Thirteen percent of all family practitioners were prescribers of chloramphenicol and this rate rose to 21% among rural family practitioners. Increased chloramphenicol prescribing was noted among rural specialists. In a separate study it was noted that relative isolation from consultation was a characteristic of more frequent prescribers.

The total number of children less than eight years old in Tennessee was estimated to be 550,000 as of 1 July 1974. During the two year study period 58,639 children less than eight years old (approximately 10% of such children in the state) received 334,128 prescriptions through the Medicaid program (Ray et al, 1977). Antimicrobials were the largest single category of drugs totalling 134,126 prescriptions (39%). Tetracyclines were the fifth most frequently used group of antimicrobials with 7,046 prescriptions (5.3%); they were preceded by ampicillin (40%), erythromycin (18%), and penicillin (18%). Pediatric syrup constituted 84% of the tetracycline prescriptions.

Prescribing patterns in the New York City Medicaid program have been reviewed by Rosenberg et al, (1974). A sample of 5,271 legend drug prescriptions and over-the-counter pharmacy orders submitted to the New York City Medicaid program was analyzed. The distribution of medication supplies by category is presented in detail. To facilitate comparisons the study utilized the clearly defined therapeutic categories of the formulary of the American Society of Hospital Pharmacists. Although no other recent study of the total prescription pattern for a low-income population existed, the distribution observed basically paralleled the findings for general populations. Specific areas in which differences were noted related to the structure of health care services for New York City's indigent population and to desirable decreased prescribing of abusable items for which the New York City Medicaid program required prior authorization.

7.3 Drug Use In Children

Drug use in children, as with other populations, is of interest because of the seemingly high incidence of infectious diseases and accompanying use of anti-infectives and other medication for what, in many situations, might be only minor disorders. Cleary (1976) examined the prescriptions for patients under 15 years of age issued by some 116 general practice U.K. physicians. Among the findings was the fact that prescriptions for this age group represented 18 percent of the total prescribed items; although the proportion of these patients to the total patients examined is not reported. The top 80% of these prescribed drugs comprised 15 therapeutic classes. Most frequently prescribed were systemic anti-infectives which comprised one third of the total, with the penicillins being the principal class of drug here.

In another British study, Catford (1980) looked at the frequency with which physicians prescribe drugs inappropriately for children. Using a random sample of 72 general practitioners' prescriptions, he scrutinized for drugs contraindicated in children - such as chloramphenicol, barbiturates, tetracycline, and those affecting appetite. From a total of 6331 prescriptions, only about 1% of the prescriptions could be questioned. However, Catford indicates that 42% of the physicians did use drugs that have recently been considered to be undesirable such as those to control symptoms of diarrhea, vomiting, and enuresis. Generally, it was found that most drugs that were long considered hazardous or undesirable were not prescribed, inappropriate prescriptions were infrequent, and prescriptions mostly ordered only one drug.

Sharpe and Smith (1983) investigated the drug use of children in two counties of Mississippi whose families were enrolled in the Aid to Families with Dependent Children Program. Interviews were completed in 540 households containing 1616 children, with 80.9% of them black. The range of ages was newborn to 17 years with the median age 8.5 years. 13% of the total number of children had taken one prescription drug and 21.5% had taken at least one over-the-counter drug in the previous two weeks. Over 75% of the prescriptions were new and 61.2% were paid for by Medicare. Analgesics, cough and cold remedies, vitamins and anti-infectives accounted for 75% of drugs used. The researchers were of the opinion that their data do not indicate a high level of drug use in this population; as in the two week period studied, only one of eight children received a prescription drug and about one in five children an over-the-counter drug.

7.3.1 Drug Use in Newborns

There are also reports in the literature that deal with drug utilization in the newborn. Drug use appears to be similar to older children relative to the general exposure to drugs. For example, Aranda and workers (1976) first examined the data from 331 newborns admitted to a newborn intensive care unit in Montreal and later studied some 293 newborns (Aranda et al, 1982). In the latter study, they showed that 76.1% of the newborns received 1-26 different drugs averaging 6.19 drugs per baby. Most commonly used drugs included antibiotics, calcium gluconate, sodium bicarbonate, furosemide and vitamins. These data find use by themselves and also in identifying future research priorities and educational programs designed for health workers who deal with drugs and the newborn.

Russel and McKenzie (1983) surveyed 265 neonatal intensive care units in the U.S., but received only 62 questionnaires for a return rate of 23% representing some 25 states and the D.C. area. They were interested in: a) establishing what medications were currently used in these units; b) determining common doses and methods and rates of administration; c) determining incidence of phlebitis associated with intravenous use; and d) what medications were added to hyperalimentation solutions. Their report carries several tables that answer these questions and suggests that the Pharmacy and Therapeutic Committee require dosages for commonly used drugs be specified in a reference notebook and be available to all concerned with drugs in this type of setting.

7.3.2 Hospitalized Children

Moreland et al (1978) describes a study of drug prescribing for hospitalized children in Scotland. They collected data for 2 calendar years from prescription forms of almost 60,000 patients, finding that there was greater use of antihistamine/sedative, anticonvulsant, and decongestant/ mucolytic drugs in children than in adults. Antimicrobials accounted for about one-third of the total drugs used in children, and one-half of all patients received at least one drug from this category. Penicillin preparations accounted for 65.1% of all antimicrobial drugs.

Stanulovic et al (1984) illustrates two important points in the area of pediatric drug use. They raise the issue that in certain areas of drug therapy for children, unexpected discrepancies may arise between accepted therapy and behaviour of prescribers. They cite the use of procaine benzyl-penicillin causing two fatalities. In another example, they point out the relationship between the use of antitussives and other drugs in the symptomatic treatment of respiratory diseases in outpatients and inpatients. The pressure of unduly optimistic expectation of therapy imposes a high prescribing rate of these products in the outpatient population, contrasted to hospitalized patients whose physicians prescribe antitussives less often due to less pressure to do so. Lastly, they demonstrate the possibility of inadequate education in antimicrobial use by citing that doctors in regional hospitals use choramphenicol ten times more per bed-day than colleagues in a university hospital, even though the regional hospital doctors received their training in university hospitals.

7.3.3 Emergency Room Drug Use

Quality of prescriptions issued in a pediatric emergency room is an issue considered by Wingert et al (1975). It is really a question of compliance with the parent responsible for administering the drug based on often incomplete directions from the physician. The researchers examined 4,364 prescriptions written by 18 physicians for 2,403 patients, and dispensed by 9 pharmacists over a 32 day period. Only 5% of 2,213 prescriptions reviewed for quality evaluation were error free. The other prescriptions had some sort of error due to quantity, dosage, time interval, hours for administration or instructions. It appears that there is room for improvement by both physicians and pharmacists in writing and dispensing prescriptions, such that the patient is able to take the drug in a more appropriate fashion.

Guidelines for the safe and effective use of drugs in children can only be formulated on information based on risks and benefits found in clinical practice. This type of information for a pediatric population has been gathered through the means of a collaborative effort between the Clinical Pharmacology Unit of the Children's Hospital Medical Center and the Drug Epidemiology Unit of Boston University Medical Center.

Mitchell et al (1976) report that the methodology invokes two levels of capture. First, acute effects of the drugs are monitored during hospitalization and second, by "viewing the hospitalization itself as the possible consequence of drug therapy".

The authors point out the fact that "children have a risk of drug therapy in addition to that encountered by adults, in that they are susceptible to alterations in growth and development. It is, therefore, particularly important that we be able to identify the long-term effects of medications used in children." The following objectives were set out relative to giving drug information on children:

a) description of patterns of drug utilization;

b) quantification and evaluation of known adverse effects of drugs;

c) detection of previously unknown effects of drugs, including drug interactions;

d) evaluation of the role of patient factors that influence drug toxicity and efficacy;

e) the provision of a methodology and structure capable of incorporating various clinical trials without significant alteration in program design; such trials might evaluate currently used drugs, new uses for currently licensed drugs, or drugs in premarketing phases;

f) the provision of a data base to enable evaluation of the various methods of pediatric dosage calculation; and

g) the establishment of a large, comprehensive data base relating to drug use in the pediatric population, to be used for a variety of clinical, pharmacological and epidemiological evaluations.

The methodology was developed from that used to monitor adult populations. Specifically, trained nurses record relevant data of a medical history nature. "Dosage, indications for use, frequency and other relevant data are obtained on all drugs administered in the hospital and adverse reactions, if any, are recorded." Other data related to events occurring in the hospital, but not attributed to drugs, such as fever, are recorded also.

Of 800 patients studied, data exist and were completed for 556. The average age is 8.0 years with 24.6% of patients being less than one year old. 55% of the population was male and mean hospitalization time was 7.8 days. An average of 6.9 different drugs were given to patients in the hospital.

7.3.4 Drug Use in Ambulatory Children

As almost all of the research of pediatric drug use takes place in a hospital, it is useful to learn of similar use in an ambulatory population. Kennedy and Forbes (1982) conducted such a study in 1979. They found that anti-infectives and cough and cold preparations accounted for about 50% of the drugs used. Tetracycline continues to be used despite its potential for problems and contraindications in pediatric use and despite the advantages of amoxicillin, ampicillin is still widely used.

The question of tetracycline use in children seems to be quite clear in that it is should not be used in children who are under the age of eight years. It is somewhat interesting to learn that in the year ending June, 1963 more than 13,000 kg or about 15 tons of tetracycline in liquid pediatric dosage forms were certified by the FDA (Jaffe et al, 1966). Tetracycline is not really a drug of choice in common pediatric infections and its only use here would be where other drugs are not likely to be effective or are contraindicated. Indeed, the Department of Pediatrics of McGill University and of the Montreal Children's Hospital voiced concern in a letter to the Canadian Medical Association Journal urging that the marketing of oral pediatric preparations of tetracycline be prohibited (Utter, 1974).

A possible explanation for the continued availability of liquid tetracycline preparations is put forward by Ray et al (1977a). They suggest that geriatric patients might require it as they could experience difficulty swallowing capsules. However, using medical data from Tennessee, they found that 55% of the prescriptions for syrup and 96% of the prescriptions for drops were for children less than eight years old. An additional 22% of syrup prescriptions were for children 8 through 14 years of age. Further investigation of the diagnosis for these children showed that 74% of the prescriptions were for upper respiratory infections and an additional 5% for pneumonia. It is the impression of these researchers that some three-quarters of the prescriptions for liquid tetracycline were inappropriate. The same authors (Ray et al, 1977b) report on tetracycline prescribers to ambulatory children. They indicate that physicians in family practice prescribed the greatest quantity, and that surgeons and internists prescribed more tetracycline to young children than did pediatricians. By comparison, rural family practitioners were the greatest tetracycline prescribers.

Another problem in pediatric drug use is that of polypharmacy - the excessive use of concomitant drug therapy. Stickler (1980), documents this issue well with an extensive bibliography. He suggests that the responsibility lies with the medical profession and indeed with the medical educator.

Lastly, the use of acetaminophen and aspirin is discussed by Mitchell et al (1982) who studied 3,587 hospitalized children between 1974 and 1979. They found that there was a decreased use of both drugs for the treatment of fever in children, and conclude fever is a less frequent indication for antipyretic drug therapy.

7.3.5 Antibiotic Drug Use in Children

Many studies have indicated the wide extent to which antibiotics are used in children and noted the need for care in prescribing this class of drug. Principi et al (1981) describes a computer system to record and analyze antibiotic prescriptions for hospitalized children which seems to be an outgrowth of a previous study (Principi et al, 1979). The system is organized to obtain, simultaneously, a quantitative evaluation of antibiotic use and a qualitative analysis of the physician's decision process for therapy choice.

The system has been demonstrated in nine different pediatric wards, analyzing 765 prescriptions. Errors have been discovered such as basing therapy only on clinical impressions in 31.5% of the prescriptions. Rational choice was found in 20.1% of the situations, and dosages were compatible with good practice in 22.4% of the cases. Lastly, they found that the physician's attitude about laboratory monitoring of side effects was adequate in 52.8% before treatment and 33.4% during treatment. As the physicians completed the computer cards at the time of therapy selection, the data reflect a fairly accurate picture.

Tolentina (1979) has observed variations in the use of antibiotics in a pediatric hospital in Italy indicating that variations in use do occur and suggesting that choice of drug is not always rational. Also, Schollenberg and Albritton (1980) reviewed antibiotic use at a pediatric teaching hospital for a month, noting errors in therapy. They found an error rate of 30% in medical orders and 63% in surgical orders, with the most frequent error being unnecessary therapy discovered in13% and 45% in medical and surgical orders respectively. Error rates were highest for most frequently ordered antibiotics - the penicillins.

Faden and Eddy (1980) cite other research that reports nearly one third of hospitalized patients receive one or more antibiotics which, upon critical examination of use, suggests that 30-60% of the medications are either unnecessary or inappropriate. In addition, excessive use is expensive, creates the potential for adverse reactions, and affects the microbial environment of the hospital significantly. By studying patient charts, these authors conclude that prophylactic antibiotics were used as frequently in pediatric surgical patients as has been reported in adult patients. They suggest that differences between the two populations must be taken into account when establishing criteria for appropriate use.

Naqvi et al (1979), in a similar type of study, confirm the above results. They found that 67% of antibiotic therapy given to children on surgical wards is in some way inappropriate - usually no indication for use, wrong drug or dose, or inappropriate timing.

The extent of antibiotic use in children is described by Grace and Goulds (1980). These workers examined records of children born between November 1, 1973 and October 31, 1974 and created a data base of 92 children who had not yet reached their fifth birthday. 33% of their prescriptions were for antibiotics and 31% for an antihistamine or cough syrup. 96% of these children received at least one course of antibiotics and the average child 4.5 courses.

An attempt to examine rationality of antibiotic use was conducted by Gibbs et al (1973) who examined the antibiotic therapy of 167 pediatric patients. They assessed the therapy by determining whether signs or symptoms of infection were present. Cultures were taken and pathogens grown. They found that rational therapy, according to study definitions, measured 32.3% and irrational therapy as 19.2%, with the quality of therapy being due partially to the level of culturing and sensitivity testing.

7.3.6 Over-the-Counter (OTC) Drug Use in Children

Pharmacists are becoming more involved in direct patient care. One area that is well suited to this role is with OTC drugs. With this opportunity to counsel consumers of these products comes the opportunity to counsel parents who select OTC drugs for their children. Because children's physiologic and pharmacologic responses differ from those of adults, pharmacists must remain alert to question parents appropriately and not hesitate to recommend professional medical attention when it is thought to be necessary. Masaki (1975) deals with these issues from the point of view of differences in children's ability to metabolize and excrete medication and by providing some useful and practical tables.

Bryant and Mason (1983) questioned parents of pediatric patients, by means of a questionnaire, about the selection and use of non-prescription drugs for their children. The questionnaires were distributed to 200 hospitalized patients one week before hospitalization to collect data on the previous six month periods. They received a response from 160 respondents and found that 97.5% of the children were self-medicated by their parents within six months of hospitalization. Only 21% of the parents accepted advice before deciding to medicate their children. Physicians, pharmacists and other health professionals respectively were sought as advisors, leading the authors to conclude that pharmacists should take a more active role in this area.

7.3.7 Comment

For some time, particularly since the thalidomide tragedy in the early sixties, medical authorities have argued for restraint when ordering drugs for pregnant women. We have seen from the literature that medications prescribed for pregnant women do not differ from those ordered for non-pregnant women. Perhaps the greatest change is that with the use of tetracycline. On the other hand, even though it is rarely a drug of choice and is contraindicated in children under the age of eight, tetracycline continues to be produced and used in alarming quantities.

Researchers have reported on studies that have examined drug use in ambulatory children, pediatric emergency rooms, on hospital wards, and in newborn intensive care units. The findings seem consistent in that there is extensive use of antibiotics, and in some cases the use of this category of drug is highly questionable.

Over-the-counter drugs are not immune to being used in the pediatric patient. Of particular importance here is the recognition that pediatric patients metabolize and excrete drugs differently from adults, and this has significant implications as to how drugs should be used in children.

Certainly, few would find fault with judicious and rational use of antibiotics in children. However, the literature is full of reports of misuse and inappropriate prescribing of these products. Systems, both manual and electronic, have been developed to monitor drug use, but unless they are used consistently, little advantage accrues because of them. From the results of monitoring drug use in children, it is clear that the exposure to potential adverse reactions is high, costs increase, and hospitalization increases.

Lastly, the effects of research that have pointed out the risks and problems of drug use have surfaced in a positive way. There appears to be a decrease in the use of acetaminophen and aspirin in children for the treatment of fever. What is needed, however, is continued research in the area of drug review as it pertains to children, and particularly as it pertains to rational prescribing and intelligent use of drugs.

7.4 Drugs and Mental Health

7.4.1 Psychotropic Drug Use

The last three decades have witnessed an increase in the availability of new drugs, especially psychoactive drugs. There is a large variety of barbiturates, tranquilizers, antidepressants, stimulants, and mood modifying agents available. During the 1930s there was widespread misuse and abuse of therapeutic agents that reached all segments, ages, and classes of society. While much of the experimenting of drugs has disappeared, misuse and abuse of certain agents still abounds. The extent to which psychotropic drugs are legally available and the manner in which they are used is of interest to health workers and researchers.

Hemminki (1982) describes two problems associated with measuring psychotropic drug consumption in Finland and Norway. The first problem concerns the classification of 'psychotropic' because the definition of what constitutes psychotropic drugs is not clear. The second problem deals with the unit of measurement. Traditionally, units of measurement were expressed as: the "number of prescriptions; the weights of the drugs; the number of packages, tablets or other dispensing forms; the number of people buying or using drugs; or the amount of money spent on drugs". A more recent approach to a unit of measurement was developed in Norway in the early seventies and is referred to as the defined daily dose (DDD).

The DDD is identified for each active substance studied. Selected by experts, it is the dose, usually in grams, which is the average daily adult maintenance dose for routine use in the assumed major indication. The amount used (established by annual sales) is divided by the DDD. The resultant number of DDD can be divided by time and population to obtain the number of these doses per 1000 inhabitants per day. This, then, represents an approximate estimate of the proportion of the population receiving the drug.

The concept is workable but not without problems. A major problem arises when consumption data for different drugs are added together. This occurs if a drug is used in different doses for more than one indication and if the relative frequency of drug use for these indications varies between the areas or periods compared. In order to compensate for this inherrent error, a supplementary unit, the defined exposure dose (DED) was introduced. DED is intended to estimate the potential extent of the population's exposure to a drug.

In summary, it is apparent that one must understand the method used to compare drug use (in particular the use of psychotropics), as it may have a sizeable effect upon conclusions. Hence, figures obtained using DDDs should not be considered as facts, but rather as estimates of the underlying phenomenon.

Prior to the study conducted by Cooperstock and Parnell (1982), little Canadian data on psychotropic drug use existed. In their study they discuss U.S., Australian, Canadian and European tudies on licit psychotropic drugs. Generally, Canadian data tend to follow that of the U.S. In Canada more women than men receive and report use of psychotropics and this use tends to increase with age. Interestingly, general practitioners prescribed the largest proportion of psychotropic drugs.

The increase in psychotropic prescriptions during the 1960s and 1970s is documented by Williams (1980a & b) in his study of the epidemiology of prescribed psychotropic drug use. He points out that large numbers of people are consuming these drugs and that the risk of dependence appears to be small. There is some evidence, however, to suggest an association between tranquilizer use and road accidents (Skegg et al, 1979). However, it has been shown that alcohol use is the major substance associated with accidents. In addition, tranquilizers used with alcohol are often implicated in suicide and suicide attempts.

Keeler and McCurdy (1975) reported on the experience in South Carolina where benzodiazepines and hydroxyzine were removed from the state Medicaid formulary, while other drugs having an antianxiety effect remained available. The objective of this action was to save money and had nothing to do with the regulation of medical practice. The study evaluated how physicians reacted to this change and results revealed that no substitution was made for about two-thirds of the deleted drugs. The only explanation that seems plausible is that these ataractics are widely prescribed because of their lack of significant side effects and low incidence of addiction.

7.4.2 Hypnotics

Boethius and Westerholm (1976) investigated the purchase of hypnotics, sedatives and minor tranquilizers in Sweden in 1973. They found that benzodiazepines dominated the prescribed drugs examined, followed by barbiturates. They did not, however, know why these drugs were prescribed and to what extent they were taken. Based on the data analyzed, they concluded that the risk of an occasional user of these drugs becoming an abuser is quite small.

A Canadian study on the use of psychoactive drugs by adults was completed in Toronto by Fejer and Smart (1973). They interviewed 1200 subjects for 40 minutes each in 1971. Their sample compared well with the age and sex data for the general area. The findings indicate that 23.8% of the sample received at least one prescription for psychoactive drugs in the year previous to the interview. Most prescriptions were for females, and younger subjects (18 and 19 years of age) received fewer prescriptions than those over 60. Fejer and Smart estimated the prescription rate to be 76 per one hundred adults, which is slightly lower than what is reported in other North American studies. Tranquilizers were the most commonly used psychoactive drugs, followed by barbiturates.

The relationship between sociodemographic factors, health status, and the use of prescribed drugs was examined by Wells et al (1985) using data from the Rand Health Insurance Experiment in California. The data were a random sample of "the non-aged, noninstitutionalized, civilian population in six U.S. cities" obtained from a self-report questionnaire. The major findings, which were consistent with other studies indicated that women are approximately twice as likely to use both prescribed tranquilizers and sleeping pills as are men. They also observed that there is a greater use of tranquilizers for older enrollees of the plan.

In a follow up study, Boethius and Westerholm (1977) looked at the purchase pattern of psychotropic drugs in 1975, in individuals who obtained hypnotics, sedatives and minor tranquilizers in 1970. The authors considered their sample of 16,000 people to be representative of the population. They divided the sample into three groups based on the number of purchases: Group A represented persons who purchased these drugs only once in 1970 (representing the occasional user); Group B represented persons who purchased these drugs two to six times (representing intermediate users); and Group C represented persons who purchased these drugs seven or more times (representing the regular user). The resultant data show that "for each group as a whole there was, five years later, a highly significant intraindividual reduction in the purchases of these drugs as well as other psychotropic drugs". However during the study period (1975) both benzodiazepine and antihistamine use increased.

Increased exposure to drugs creates a greater risk of problems for the consumer. Among these problems is self-poisoning which could result in suicide. Hawton and Blacktock (1977) have looked at this from the point of view of overdosing in relation to psychotropic drug prescribing in general practice in Oxford. They interviewed 130 patients most of whom had overdosed and for 122 patients, their general practitioner was also interviewed. Apparently it is not uncommon for patients who attempt suicide to contact their physician beforehand. Of all the patients who attemped suicide 63% had seen their physician in the month preceeding the attempt and 36% had done so the preceeding week.

The basic problem underlying the misuse of psychotropic drugs might lie with the availability of psychotropic drugs to patients with psychosocial problems. This being the case, prescribing habits should be scrutinized closely and efforts should be made to change the frequency of prescribing. Care in diagnosis must be taken and drugs should be prescribed only where there are definite indications. In some cases prescribing may not be the most appropriate action; instead, alternate means such as counselling may be more beneficial.

7.4.3 Self-Poisoners

Prescott and Highly (1985) examined drugs that were prescribed for self-poisoners. They found that the use of psychotropic drugs increased progressively with age and most overdoses occurred with prescribed drugs. The availability of the drugs seems to be the problem, as one-third of the patients exhibited normal personality and no psychiatric illness. Nearly half of the patients in the study, however, did have alcohol or drug problems, and most of the unemployed patients received psychotropic drugs. Benzodiazepines were the most commonly prescribed drug. The authors concluded that more care and restraint is needed in the prescribing of psychotropics by physicians.

The prevalence of psychotropics and their use is not confined to North America or Europe. Wilcox (1977) indicates that, from analyzing more than 25,000 prescriptions in New Zealand for a five month period in 1976, one out of eight is for a psychiatric symptom. He points out that of these three quarters are prescribed to adult women, and that consumption of these drugs is greater in the urban environment.

Monitoring the use of drugs of a psychotropic nature appears to be lacking. Dennis (1979) looked at the phenomenon of repeat prescribing. From a population of over 100,000 patients, over 1000 repeat prescriptions for psychotropics were given without the physician seeing the patient. Length of time of prescription was directly related with age and inversely related to closeness of monitoring by general practitioners. Again, benzodiazepine use was frequent and women received more psychotropic drugs than men.

7.4.4 Polypharmacy

Both polypharmacy and unnecessary prescribing are seen as reasons for the extent of psychotropic drug use. Tyrer (1978) examined this question by investigating patients who were referred from general practice to an outpatient clinic over a four year period (1974-1977) in Southampton, England. Among these findings are the long term use of benzodiazepines and barbiturates, incorrect prescribing based on pharmacological grounds, and polypharmacy with drugs of similar pharmacological action. Apparently polypharmacy is common in psychiatric practice, and reflects a disturbing level of ignorance of pharmacological action among those who prescribe drugs for psychiatric problems.

Patterns of psychotropic drug use have been described by Altmax et al (1972) in Missouri, Williams (1983) in England, and Balter et al (1974) and Madsen et al (1979) in Australia. The major findings were: the lack of compatibility between diagnosis and appropriate drug choice; the increasing number of prescriptions for psychotropics; the proportion of women who had used psychotropics relative to men; and the over representation of older persons among users in relation to their presence in the population.

7.4.5 Prescribers and Consumers

The question of who prescribes psychotropic drugs was addressed by Davidson et al (1975) in North Carolina. By collecting data from patients' charts in a teaching hospital, they examined the prescribing habits (for psychotropics) of internists, surgeons, and gynecologists on inpatient wards were examined. Although it may appear strange that specialists other than psychiatrists are prescribing psychoactive agents, it is quite reasonable considering the relationship between a psychiatric condition and a physical illness. This is the first comprehensive report that deals with psychotropic drug use in general medical and surgical wards.

Results reveal that minor tranquilizers were prescribed most often followed by major tranquilizers, barbiturates and antidepressants. These drugs seem to be used uncritically, with few recordings to either identify the disorder for which they were intended, or to indicate their effectiveness.

Swett (1979) reports on a study conducted in psychiatric inpatient wards in Massachusetts. The mean number of drug exposures was 5.1 per patient with the most commonly used drug being chlorpromazine which was prescribed for 39.5% of the patients. Drugs other than psychotropics included chloralhydrate, aspirin, and milk of magnesia, being given to 28.7%, 21.2% and 11.0% of patients respectively.

Consumption of mood-modifying drugs in a Canadian city is described by Cooperstock and Sims (1971). The data sample covered 2 one week periods six months apart in 1963 and 1966. The drugs were prescribed by physicians to an outpatient population. The research found that mood modifying drugs made up 25% of all prescriptions dispensed to a non-hospitalized urban population. Sedatives and hypnotics were the most commonly prescribed mood-modifiers. 70% of these drugs were prescribed by general practitioners and only 5% by psychiatrists. Younger physicians (i.e. those graduating after 1950) tended not only to prescribe more and for shorter lengths of time, but also prescribed more tranquilizers and fewer barbiturates than other physicians.

The literature seems to be consistent in its observation of over use of psychotherapeutic drugs and in its calls for reduced use, increased monitoring, and rational prescribing.

James (1983) conducted a study whose objective was to reduce drug use in a mentally retarded population. Using the 1981 British National Formulary, he compiled a set of guidelines for drugs acting on the central nervous system, stressing the following: a) the need to avoid polypharmacy; b) the reduction of the frequency of administration of drugs; c) a reduction or discontinuation of medication unless there is evidence that it is doing some good. Regular monthly reviews of patients' medication were already in practice in the hospital and the guidelines were applied during these reviews. Reduction in the frequency and amount of drugs given was achieved, the number of drug administrations was reduced from 2.3 to 1.2 per patient per day. There was also a reduction in the number of patients on drugs, demonstrating that a regular and systematic application of guidelines for prescribing and monitoring drugs can bring about substantial reduction in their use.

Another study that looked at pharmacist impact on drug use in an institution for the mentally retarded, suggested several reasons for utilizing a pharmacist in this situation. These included a better staff-patient ratio, reduction of polypharmacy, better detection and prevention of adverse drug reactions, and up to date drug information (Ellenor and Frish, 1977).

In this two year study the pharmacist reviewed the patient's and pharmacy records to generate a drug history, and visited the patient to determine current problems, effectiveness of therapy, and the presence of adverse reactions. Recommendations were then made to a behavioural review committee. A reduction of 18% in the use of antipsychotic drugs, 50% of anti-anxiety/antidepressant drugs, 58% of sedative-hypnotics, and 65% of miscellaneous products was shown. Dollar savings were achieved while a maladaptive behavioural test indicated that decreased drug use did not significantly change behaviour.

In another study, de Graaff (1983) demonstrated that drug use reduction can be achieved in an outpatient population. It utilized a multidisciplinary approach that included a task force consisting of four family physicians, a pharmacist and representatives from nursing, social work, and mental health disciplines. The concern in this study was with the use of tranquilizers. The task force defined proper and improper use, investigated the degree of misuse, determined goals, and implemented an educational program to achieve these goals. Results reveal that the program did influence the behaviour of general practitioners. They prescribed tranquilizers less readily, and when they did, it was in smaller doses and for shorter periods. In addition, they paid more attention to the underlying problems and attempted to motivate patients to seek the help of others such as social workers.

Another approach to reducing or discontinuing antipsychotic medication is described by Kurucz and Fallon (1980). They implemented a program in a 30 bed inpatient ward for schizophrenic patients in a New York State hospital. These patients had been hospitalized for 5 or more years. A six month follow-up showed that seven of fifteen patients were still not taking medication and two improved sufficiently enough to be discharged. At a one-year follow-up, another patient was discharged after 11 years of hospitalization. The authors conclude that patients who might benefit most from reducing or discontinuing medication are over age 50 and have been hospitalized for about 15 years.

7.5 Women (see also Section 7.4)

The drug utilization literature is filled with reports suggesting important differences in the patterns of drug prescribing to women and drug use by women. In North America there has been particular concern with the use of psychoactive drugs such as anxiolytics, sedative-hypnotics, other mood-altering drugs, which are used approximately twice as much by women as men. A large number of reasons have been proposed to explain such dramatic differences; for example: health and illness behaviour of women compared to men; frequency of visits to physicians; the fact that most physicians are males; greater incidence of anxiety or depression; the likelihood that women will express emotion compared to the probability males will, etc. The importance of these reasons and the patterns of prescribing and use of drugs by women is clearly an issue of social and medical importance. Major initiatives are needed to better understand such phenomena and to develop alternative treatment strategies other than drugs when such other treatments are known to be effective and when drugs are not appropriate.

7.5.1 Drug Use in Pregnancy (see also section 7.7.3)

While pregnant women are encouraged not to consume any medication, except those that are absolutely necessary, it is well known that they do consume both over-the-counter and prescription drugs. Stortz (1977) administered a questionnaire to 100 in-hospital postpartum women in an attempt to elicit their use of unprescribed drugs. She found that 97% of the subjects used at least one unprescribed drug prior to pregnancy and 88% used at least one drug during pregnancy. The apparent decrease in drug use during pregnancy is considered appropriate, but better consumer education about the potential hazards involved is still required.

Hill and co-workers (1977) also examined the use of over-the-counter drugs in pregnant women. They interviewed 231 pregnant women between 1969 and 1975 concerning the number of kinds of drugs they consumed. They found a range of 0-37 drugs with a mean of 15.6. Prescription drug use ranged from 0-28 with a mean of 6.4 per patient and over-the-counter drugs ranged between 0-12 with a mean of 3.2 The types of drugs consumed were represented by vitamins and minerals, analgesics, antacids, iron preparations, laxatives, nasal decongestants and antihistamines.

Rayburn et al (1982) interviewed a total of 245 patients at two university affiliated hospitals over a two month period in 1982. They found 115 different drugs (prescription and over-the-counter) to have been consumed by these women. The average number of drugs per patient was 2.9 with a range of 0-7. Excluding dietary supplements, 75% of the patients took one or more drugs while pregnant and 67% took two or more drugs. There was greater drug use in the second and third trimesters than in the first trimester of pregnancy.

Physicians and in particular obstetricians, should be well aware of the potential hazards of drug administration. Brocklebank et al (1978) investigated the question of whether medications prescribed for women change as a result of pregnancy. Using medical data from Tennessee, they examined the files of 2,528 pregnant women. Of this sample, 62% received systemic drugs which required a prescription, excluding dietary supplements. Systemic anti-infectives were the most frequently prescribed category. 25% of these women received narcotic-containing medication and 13% received psychotropic drugs, usually diazepam. The study concludes that prescribing did not decrease as a result of pregnancy.

Perlin and Simon (1979) reviewed the pertinent literature in an attempt to shed light on drug taking behaviour of pregnant women. They examined the concept that social conditioning and emotional reactions to pregnancy and childbirth are responsible for drug taking behaviour. They appear satisfied that "prescribed and self-administered instances of drug use are relatively common among pregnant women and the data are compatible with a conditioned drug use behavioural pattern."

7.6 Institutions

Drug use review is not new to hospitals. They have been methodically assessed for some time, the main aims of the process remaining as monitoring standards of drug use and costs of drugs. In many instances antibacterial agents have been studied because of their widespread use, cost, and unacceptable rates of inappropriate prescribing.

7.6.1 Hospitals

One of the possible reasons for the availability of drugs in hospitals is the "p.r.n. order." This order to administer drugs "when required" essentially transfers part of the drug giving decision from the physician to the nurse. Usually included here are indications such as sedatives, antacids, laxatives, and analgesics. Ryschinsky (1978) examined the role of the p.r.n. order in relation to achieving a satisfactory level of patient care. This included an attempt to determine what proportion of p.r.n. orders were utilized inappropriately.

The study found that these orders constitute roughly 35% of all drug orders in the hospital where the study occurred. Most of the drugs, 40.1%, were analgesics while only 6.8% of the p.r.n. orders were intended as a component of the patient's primary disease therapy. Inappropriate use of these orders was difficult to ascertain but the study did find about 25% of parenteral analgesics to be questionable regarding dose or dose interval.

The use and monitoring of antimicrobial drugs in hospitals is widely examined. They are used therapeutically and prophylactically in large numbers and sometimes irrationally. Hospitals and other institutions that house patients must be vigilant for organisms resistant to current agents in order to attain effective therapy and infection control.

Examples of these types of studies include one by Greenlaw (1977) who described a program that includes the monitoring of culture sensitivity, antimicrobial and aminoglycoside use, as well as physician consultation with the pharmacy and reporting the results to the medical staff. In another study, Shapiro (1979) examined patterns of prophylaxis and concluded that limiting prophylaxis to the first 24 to 48 hours (as currently recommended) would substantially reduce antimicrobial drug costs in hospitals. Castle et al (1977) demonstrated that 34.2% of all patients at Duke University Medical Center in June, 1973 received antibiotics, many of them not indicated or inappropriately administered in terms of dosage. McGowan and Finland (1974) conducted a study, collecting data at three year intervals between 1964 and 1973 at the Boston City Hospital. They examined the prevalence of infection and usage of antimicrobial agents finding "an increased proportion of patients receiving antimicrobial agents and decreasing use of therapy with more than one antimicrobial agent in the same patient." Adler et al (1970) conducted a follow-up to this study in 1970. Twelve percent of the patients had hospital acquired infections and this did not differ greatly from the previous data.

Drug utilization has been examined in many contexts and in many practice sites. Buchanan and Cane (1978), for example, studied 200 patients in a general intensive care unit finding 102 different drugs prescribed with a mean of 7 per patient. They point out the potential for polypharmacy and drug interactions. Corrigan (1983) reported on drug use in an Irish Orthopaedic hospital, where as one might expect, 41.5% of patients consumed anti-inflammatory agents.

His major interest in this particular study, however, was night sedative consumption and he found that the use of barbiturates declined from 40% to 2% of sedatives used. The major sedatives, 95% of all used, were nitrazepam, flurazepam and diazepam. Another example of drug use review in a hospital setting is provided by Hall et al (1981). They examined the use of cimetidine in a large Canadian teaching hospital concluding that it was used in indications for which it was approved and in some instances for indications where it was not approved. In general, 80% of the patients received the drug for treatment and 20% for prophylaxis.

As one of the purposes of drug use review is to increase rational drug use, intervention into current systems of drug distribution are necessary. May et al (1974) explored this issue in which they studied 7,575 patients over a 3-1/2 year period. They found that a formulary had a definite impact on drug use and cite the example of propoxyphene as a formulary drug. When it was included, about 40% of patients received it, when it was removed from the formulary, its use diminished to less than 1%.

Education is another strategy used to intervene in the drug distribution process in an attempt to affect drug giving behaviour. Johnson et al (1982) illustrate an example of this type. They used predetermined criteria for acceptable use of gentamicin in a hospital. In the pre-education period, 52% of gentamicin causes of therapy were found acceptable; and following an educational program, this was increased to 78%.

7.6.2 Drug Use in Non-Hospitalized Settings

Outpatient populations and ambulatory patients are given drugs and consume them differently from hospitalized patients. Part of this behaviour results from the setting and part from the characteristics of the patients. Lech et al (1975) described the characteristics of heavy (outpatient) users of prescription drugs. They studied a group of patients at an outpatient pharmacy in San Francisco belonging to the Kaiser-Permanente Health Plan. Although there are determinants of drug use in the patients, their physicians, and the medical care system itself, these researchers concentrated on the patient.

From the population of 29,000 receiving one or more drugs, less than 1% received eight or more different drugs during a three month period; they were deemed 'heavy users'. A random sample of 225 was selected from over 23,000 receiving only 1 or 2 drugs during the same period. Both groups were further reduced in size to include 158 'heavy users' and 99 'light users'. Heavy users were older, female (housewives) and white. If male, the heavy users had blue collar occupations. The heavy users were also associated with greater use of medical care; among them were some "severely ill persons and some with emotional problems that appeared to contribute to symptoms and request for drugs."

Part of the outpatient population obtains its drugs in an ambulatory care centre. Brassler, Stewart, and Keys (1981) discuss criteria for drug use review in such a setting. Basically, they demonstrate that guidelines for inpatient institutions such as the criteria, peer review and mechanism of developing and applying the methodology, can be modified for outpatient sites.

7.6.3 Health Centre-ambulatory patients

Gong and Floyd (1980) take the process of drug use review one step further. In a health centre pharmacy located in Los Angeles, they were interested in determining the commonest disease states of their patients, the age and sex distribution, average medications per patient, and proportion of new prescriptions to old. Using these data to build a profile of their clientele, these researchers were able to plan services that are more directly targeted to filling the needs of their patients.

Hlynka et al (1981) illustrate how a 'universal' computerized prescription record system in B.C. can be used in a drug use review process. They first of all defined the suspected problem by targeting specific drugs, defined criteria for use of the targeted drugs, and site standards for their use. Next, existing problems were identified by measuring the target drug(s) use, screening for exceptional use, and then identifying potential problems.

From this process, the authors concluded that drug use review can identify potential problems among targeted drug users. The process does not stop here but attempts to correct the problems identified. This was done through educational programs aimed at physicians and pharmacists rather than at patients. The effectiveness of the education program was measured by collecting data in the same fashion as in the pre-education phase. The pre and post-education data were then compared. The results showed a decrease in the number of patients given target drugs, in the number of patients whose use of these drugs was exceptional, and in the number of patients whose drug use was a potential problem. As well, the researchers found a decrease in the numbers of patients using the target drugs suggesting that the professionals contacted were successful in correcting many of the problems and in reducing the number of people at risk. Thus, the use of drug profiles advances rational drug care.

Another study used drug profiles to determine if drug utilization in an ambulatory setting could be improved. Sobczak and workers (1984) worked to determine the usefulness of drug profiles to physicians. Specifically, 1) would drug use data provided to the physician result in improved patient care? 2) would time be saved in reviewing drug histories? and 3) would drug duplication and polypharmacy decrease?

Use of the profiles was not mandatory and monitoring of their use was not done. Since the study took place in a veterans hospital, all drugs were provided at no cost and drugs purchased elsewhere were not accounted for. Patients who were studied had a decrease in their medications over the test period. Of those patients who had duplicate medications, 46% showed a reduction, 20%

showed an increase, and 25% were unchanged. Physicians saw the drug profiles as decreasing the time spent determining patient drug histories, but a majority viewed the histories as important in dealing with overuse of drugs.

From manual profiles, the next logical step is to move to a computer. The speed and accuracy are obvious advantages once a program is operational. Reed et al (1982) provide an example of computer-assisted, medical record audit which included prescription screening.

7.6.4 Health Maintenance Organizations (HMOs)

A number of drug use review studies have been conducted in health maintenance organizations. Essentially, these have been on ambulatory patients who have elected to belong to a prepaid health group of their selection. West et al (1977) developed and implemented a program to review drug use based on criteria from the scientific literature. They also wanted to evaluate the effect of drug use review on physician prescribing. Using a health maintenance organization in Columbia, Maryland as their research site, criteria were developed for therapeutic categories of interest using the scientific literature as a reference. Deviation from the criteria were determined by peer review and a Pharmacy and Therapeutics Committee was employed to promote adherence to the criteria.

A before and after design allowed the opportunity to determine whether changes in prescribing occurred. As an example, data for antihistamines were used to illustrate the effect of the program. A decrease in use was observed for upper respiratory infections, and in cases where combination products were deleted from the formulary.

Johnson et al (1976) explored the use of patient drug profiles to see if they influenced quantitative or qualitative aspects of receiving prescriptions. The research was conducted among persons enrolled in the Kaiser Health Plan. Interestingly, the results indicated that drug profiles did not have an influence. The researchers point out that this result challenges current thinking in this area and suggest that caution be used in their interpretation. Further, they suggest that the population served, the medical care setting, the characteristics of the profile, and the conditions surrounding its use all be taken into account as these could influence the outcomes. This study addressed the profile, but as a technique it did not address the concept of information as an aid to decision making. The emphasis here was on physicians rather than pharmacists and the researchers suggest that additional work is needed in this area.

Part of the justification of drug use reviews is to reduce the cost of dispensed drugs and increase the efficiency with which they are distributed. Hardigan, Slywka and Eng (1980) examined these concepts in a HMO in Arizona. Most prescribed items, cost of drugs dispensed, cost of drug per prescription, and number of prescriptions per enrollee of the plan was observed. The data may reflect the health status of the population being treated, and indeed, this approach may be an inexpensive way to obtain that information.

Non-medical factors associated with the volume of drugs prescribed to users of a HMO were explored by Hartzema and Christensen (1983). These types of factors provide useful information for planning in that they help forecast demand for services. The researchers point out that "knowledge of either the family practitioner or patient sex-age mix can also be helpful in planning for drug-related services (pharmacy size, drug inventory, staffing)."

7.6.5 Skilled Nursing Facilities

Nursing homes, facilities which combine residential care with difficult levels of medical care, are responsible for a large degree of drug therapy. Skilled Nursing Facilities, nursing homes with a high degree of medical care, have been examined from the viewpoint of drug use. Of concern in these facilities is the degree of overmedication that occurs. Segal et al (1979) examined a facility in California that was attended by seven physicians. Fifty patients were selected randomly and their drug regimens analyzed. Polypharmacy was practised in 59% of these patients with non-substantiating diagnosis. More drugs were prescribed in potentially toxic doses than in subtherapeutic doses and approximately one-half of the drugs were simply administered p.r.n. (i.e. when required).

There was also risk of adverse drug reactions; highest when a drug was prescribed without a record of a definite diagnosis. The authors concluded that greater effort needs to be put forward in auditing prescribing and the care of patients.

Lamy and Krug (1978) have reported on drug use in a Skilled Nursing Facility as well. However, they have taken a specific approach and concentrated on laxative use, finding that they are the most frequently prescribed drug in this type of facility. The suggestions that more attention should be paid to the dietary management of constipation in this population, and physician education as an intervention strategy are also supported in this instance by Elzarian et al (1980) in order to decrease laxative use.

7.6.6 Nursing Homes

Nursing homes which had skilled and intermediate levels of care were compared for indications of different drug needs of the two patient populations by Hamilton (1976). The comparisons were made by examining the medical records and drug therapy recommendations of the consultant pharmacists in each facility. There was no significant difference in the types of problems identified in either patient population. Therefore, patients in skilled and intermediate nursing home facilities do not differ in the need for therapeutic monitoring by consultant pharmacists.

The need for pharmacist involvement in drug use review in nursing homes is further strengthened by Bergman's (1975) work. He reviewed the prescribing of 23 physicians who cared for patients in a 106-bed facility. The basis of evaluation was designated use of the drugs compared to FDA-approved use and with efficacy or need in each case. Only 4.1% of the drugs prescribed were considered to be not needed or ineffective. The author suggests that because only the physician reviews the patient's health status each month, this may predispose him or her to prescribe more drugs than are necessary. As a result of this speculation of cause, the study concludes that pharmacists should be involved in a drug use review program in order to promote rational drug therapy.

The Canadian experience of drug use review is documented by Danforth, Hlynka and Soon (1982). They set out a procedure for accomplishing a drug use review process for long term care facilities and tested it in 412 facilities in British Columbia. The objective of their research was to measure quantitative patterns of general drug use for administrative trend analysis. In addition, they wanted to measure the quality of use of selected target drugs for professional education. They suggest that a professional review committee structure be retained in the future to assure that the professions concerned and responsible for prescribing and dispensing drugs will control the definition of standards and corrective procedures to be used in the drug use review process.

Two other studies examined drug use in Canadian long term care facilities. The first by Segal and Bornstein (1984) attempted to document the status of provision, control and administration of prescription and non-prescription drugs in long term care facilities. They found that, in the facilities used in Metropolitan Toronto for the study, most of the patients were female and in their eighties, and that the patients suffered from a number of health problems, with cardiovascular disease being predominant. There was a high use of drugs and this in itself led to a potential for drug-drug interactions and high drug costs. Because of this situation in these facilities, the researchers suggested that there was an opportunity for more pharmacist involvement.

A follow-up study by Studnicki-Gizbert and Segal (1983) assessed the pharmacist's contribution in reducing inappropriate prescribing and administration of medication as well as looking at positive ways to reduce the cost of medication in these facilities. They were partially successful in reducing drug use and cost by working closely with attending physicians and facility staff.

The issue of implementing drug therapy reviews was discussed by Vlasses et al (1977). They described the administrative negotiations, implementation and one-year retrospective evaluation of this service, with generally a positive outcome.

The need for this type of program in long term care facilities is demonstrated because of: a) the incidence of polypharmacy (Kalchthaler et al, 1977); b) the contribution of a pharmacist who monitors therapy (Tsai et al, 1982 and Williamson et al, 1984); c) greater drug use of elderly persons in residential homes (Morgan and Gilleard, 1981); d) high rates of nonconformance to established criteria for drug use (Stewart et al, 1978); e) the potential for drug-drug interactions among the elderly (Cooper et al, 1975); f) the prevalence of "p.r.n." drug use (Aycock, 1981; Brown and Desimone, 1980); and g) inappropriate use and misuse of drugs (Ray et al, 1980 and Waxman et al, 1985).

It would appear that from the documented experiences noted above that a large amount of drug waste occurs. Patry and Kroeger (1978) in fact, have examined this issue. They looked at drug waste resulting from a traditional drug distribution system by measuring inventory levels of discarded medications. These researchers suggest that changing to a unit dose system or capitation fee system might reduce waste and a process of drug use review may reduce the number of "p.r.n." orders and ultimately reduce waste and cost.

7.6.7 Drug Treatment Centres and Outpatient Clinics

For patients who do not require constant and/or institutional care, day treatment is a cost effective and viable alternative. The question of whether specific drug control mechanisms should be established is one deserving of an answer. Of particular interest is the potential for problems coming from compliance issues and the degree of pharmacist involvement in such a facility.

Boykin et al (1978) reviewed and evaluated the medication of participants in a day treatment centre in Baltimore. They found several areas for improving patients' care, such as incomplete medical records, communication between the physicians and centre staff, and drug control. Suggestions are provided for using a pharmacist consultant who would initiate and maintain drug records as well as provide drug use counselling.

Interest in outpatient centres is also illustrated by Barsky et al (1979). They investigated minor tranquilizer use in a neighborhood health centre. The emphasis of this study was on the characteristics of the users. The population involved elderly of low socioeconomic status, and mostly single or widowed. Findings from this study indicate that chronic tranquilizer use was associated with chronic medical problems. In general, the authors point out that more information is needed on both the prescribers and the users of these drugs.

Hosek, Bacikova and Vinar (1981) were interested to learn if the pattern of psychotropic drug use varied with the patient's status: inpatient or outpatient. They found that the frequency of treatment was higher in the outpatient if they were higher in the hospital. It appears that frequency of outpatient treatment mimics that of inpatient treatment.

Another example of drug use review to outpatients is provided by Salberg et al (1983). They looked at the use of non-steroidal anti-inflammatory drugs with a view to cost reduction of therapy.

They reported a potential cost saving by restricting use of the newer drugs of this class.

7.6.8 Pharmacist contribution

The role of the pharmacist surfaces constantly in the pharmaceutical literature. One recurring theme is the pharmacist's ability to monitor drug use with the anticipated outcome of improved therapy and increased quality of care as described by Hood, Lemburger, and Steart (1975).

One innovative approach to improving patient care in long term care facilities is to reduce drug intake. Steinberg (1984) discusses how this might be accomplished and how the pharmacist might participate. She points out, however, that 'drug holidays' are not for all drugs nor for all patients, and that specific staff preparation, approvals, policies, and patient/physician acceptance of the concept are all necessary to make it work.

Kidder (1982) has made some estimates on the potential savings that can be generated in long term facilities as a result of drug use reviews. Citing skilled nursing facilities and intermediate care facilities as examples, he estimates annual savings of $25 million and $38.4 million respectively. The cost of performing these reviews is reported by other workers to be around 15¢ per patient per day or about $4.50 monthly. Kidder also suggests that there are considerable savings to be achieved from reduced hospitalization due to inappropriate drug therapy.

8. SUMMARY AND CONCLUSIONS

The need for the study and review of drug utilization practices is based on the increasing evidence of irrational prescribing, drug waste, and misuse of medications by patients in both private and public health care programs. Many studies have documented the irresponsible prescribing of certain medicines, such as proprietary analgesics, psychotherapeutic agents and expensive antibiotics, without establishing any acceptable justification for their use. Other studies have demonstrated equally irresponsible practices such as the prescribing of excessive quantities of drugs, and the collection of multiple prescriptions from different physicians for the same symptom. Reports of large quantities of unused medications in patient's homes also indicate wasteful and costly drug utilization practices.

The purpose of this section is to provide a general summary of the major observations and findings identified by the four members of the research team during their comprehensive review of the literature on drug utilization. In addition, this section will present the conclusions arrived at by the members of the team.

The members of the research team reviewed more than 2500 publications dealing with various aspects of drug utilization. They read various government and professional organization reports dealing with this subject. A comprehensive bibliography of the publications involved in the study is included as an appendix to this report. This literature included many types of research; but throughout the review it was obvious that there is a need for more research emphasizing the problems highlighted in this report. The committee strongly recommends such research to be fostered.

This final section of the review will present the views of the authors in the following question format: a) Is there a problem? b) If so, what are its components and dimensions? c) What possible solutions are there to solve the problem? and d) Is there evidence to support one or more of the possible solutions?

8.1 Is There A Problem?

The evidence seems to be overwhelming that indeed there is a worldwide problem relating to drug utilization. It is improbable that the problem is any less in Canada. Our review of the literature clearly indicates that this problem is both serious and significant. The problem involves both overprescribing as well as inappropriate prescribing. This means that in many cases: a) the wrong drugs are prescribed; b) ineffective drugs are prescribed; c) effective drugs are not prescribed; d) drugs are prescribed in inappropriate amounts or for inappropriate periods of time; and e) expensive drugs are prescribed when less expensive or even non-prescription drugs would be as effective or more effective.

The consequences are that patients do not always receive the optimal benefits from the use of drugs, which now probably represents the most widely applied form of medical therapy.

Moreover, the economic consequences of drug misuse show up in the health expenditure data for Canadians. Not only do Canadians spend a larger proportion of their total health expenditures on drugs but they also consume more drugs than do residents of other industrialized countries. Thus, even though Canadians pay less than others (e.g. the Americans and British) for the products which they purchase, expenditures on drugs represent a large proportion of total health expenditures because they receive a larger number of drugs per capita.

8.2 If There is a Problem, What Are Its Components?

The problem associated with drug utilization involves both prescribers and dispensers, as well as consumers.

8.2.1 Physicians

From the prescriber perspective, there is little doubt that there have been and continues to be problems in prescribing. These problems relate both to over-prescribing of drugs for which there is no evidence of efficacy, as well as under-prescribing of preventive medications like vaccines for unimmunized children and adults.

The reasons for inappropriate prescribing have been identified to include the following:

a) inadequate training of physicians during their medical school years on the day-to-day application of drug knowledge;

b) inadequate sources of objective information available to practicing physicians about drug properties and indications;

c) the limited time available to practicing physicians to study and evaluate the therapeutic claims for newly marketed drugs;

d) the widespread custom of physicians to continue their drug education by relying mainly on the promotional activities of the drug companies; and

e) the exceedingly rapid turnover in the popularity of prescription drugs.

8.2.2 Pharmacists

The problem for pharmacists is equally complex and equally difficult to overcome. Among the problems associated with the practice of pharmacy are the following:

a) lack of opportunity for pharmacists to realize their full potential role in the health care team;

b) lack of an adequate data system to enable an effective review system of drug utilization (including patient profiles) to be established;

c) difficulty in determining a method to accurately define acquisition costs;

d) lack of incentives to encourage pharmacists to dispense lower cost, generically equivalent products;

e) lack of uniform accounting systems in pharmacies which would enable an accurate determination of the cost of dispensing prescriptions;

f) difficulty in establishing appropriate dispensing fees.

8.2.3 Patients

Patients also play a major role in the problems identified with drug utilization. While many of these problems are related to the behaviour of both physicians and pharmacists, undoubtedly there is considerable interaction among all those involved in the process of prescribing, dispensing, and drug taking. Problems encountered by patients include the following:

a) lack of communication between physicians and their patients. This is illustrated by the fact that physicians often neglect to explain (in language that the patient can comprehend) what the drug is, what it is expected to accomplish, precisely when and how to take it and for what length of time, what side effects may occur, and what to do if they occur.

b) the response of patients to the lack of clarity of the physician's intention in prescribing the medication often results in inappropriate actions such as:

- patients who are advised to take a particular drug before meals, sometimes take it after meals;
- patients who are warned not to use alcohol while they are using a particular medication, stop drinking whiskey or gin but continue to drink beer and wine;
- patients told to take an antibiotic for ten days, stop

taking it after three days because the symptoms are apparently gone;

- some patients double the recommended daily dosage, perhaps in the belief that if three pills a day are good, six must be better,
- some patients who neglect to take the medication for three days, take quadruple the dosage on the fourth day; and
- many patients neglect to report an early adverse reaction to their physician or pharmacist, a delay which might result in serious complications.

c) there is an overwhelming problem with the fact that patients frequently do not comply with instructions on the use of drugs given by the prescribing physician. This lack of compliance, which has been estimated to range as high as 10 percent of all patients receiving prescriptions, takes a variety of forms, such as:

- in short-term illness, there is a tendency for patients to stop the medication when there is the first relief of symptoms,
- in long-term, chronic illness some patients tend to become confused, forgetful, or bored.
- when a patient is put on treatment with two, three or more drugs at the same time, there is a risk of confusion or of unpleasant side effects resulting from the interaction between the drugs, which leads some patients

to stop taking some or all of the prescribed medications.

8.3 Possible Solutions to the Problem

The literature has identified a number of possible courses of action to solve the problems associated with drug utilization. It is to be emphasized that these problems can be addressed in rational ways, and that it is worthwhile doing so, particularly from the perspectives of quality of care, patient health and cost-effectiveness. The solutions range widely from educational strategies to institutional changes to programmatic changes, among many others. Each of these is described and discussed fully in the body of the report.

The purpose of this section is to review briefly what we consider to be the most attractive options and to discuss some elements which should be considered in developing a strategic plan for dealing with the major issues.

Among the strategies which have been identified in the report, the following most frequently appear in the literature as embodying the greatest potential for confronting the problems associated with inappropriate prescription drug utilization:

a) use of limited drug formularies;

b) substantial expansion of drug utilization review (DUR) systems;

c) use of educational techniques to influence prescribing, dispensing and utilization patterns;

d) introduction of innovative payment strategies to modify incentives for the prescribing and utilization of drugs;

e) encouragement of the development of alternative health care delivery systems which embody incentives to provide cost-effective services while ensuring continued access to quality health care;

f) the use of lower cost, generically equivalent products in place of no more effective but higher priced products; and

g) an effective linkage system between diagnostic and therapeutic data bases.

8.3.1. Formularies

The issue of whether the use of a formulary is an effective method of improving the rational use of drugs has long been debated over a number of years. The debate not only involves the question of whether it is an effective method, but also which and how many drugs should be in the formulary, should its use be voluntary or mandatory, should it apply only to institutional practice or involve ambulatory care as well, and whether or not the use of formularies actually saves money.

The answers to many of these questions are far from clear or definitive. However, it would seem that the literature leans very heavily toward the proposition that the use of a formulary is an effective way of influencing more cost-effective and more rational drug therapy.

There is a widespread assumption that most hospitals, particularly large ones, make use of formularies. This assumption seems not to be justified. A fairly recent survey conducted in the United States showed that:

a) about 40% of large hospitals do not use any formulary at all. The situation is probably worse in small hospitals;

b) in some cases, it was impossible to learn the identity of the active ingredient from the formulary, from standard reference books, or even from the manufacturer;

c) sometimes a company was listed as the manufacturer of the product, but company officials denied that they had made it; and

d) although most combination products, consisting of two or more active ingredients, had been seriously criticized by the U.S. National Academy of Sciences/National Research Council, they were found in large numbers in the formularies.

We are unaware of any similar survey having been conducted in Canada. However, members of the research team were aware of large hospitals which had no formulary whatsoever, and would be surprised if a majority of hospitals, even large hospitals, made use of a mandatory drug formulary.

The situation regarding ambulatory practice is even more dismal. While some ambulatory service plans, like HSO/HMOs, have adopted and generally use a specific formulary, this is by far the exception rather than the rule. The use of formularies in ambulatory care is therefore rare; and if the use of formularies seems to be increasing, it is at an imperceptible rate, if at all.

The issue of how many drugs are required for an optimal, or even reasonable, drug formulary lacks any degree of consensus. Estimates range from just over a couple of hundred drug entities to upwards of several thousand products. The World Health Organization has proposed a basic list of 214 drugs, of which 182 were classified as 'essential' and 32 as 'complementary' (Lasagna, 1980). Many of the Scandinavian countries have adopted formularies which contain only a couple of hundred drugs. While there is no consensus on the precise number of drugs to be included, the preponderance of opinion seems to favour the lower end of the scale rather than the higher.

8.3.2 Drug Utilization Review

There is increasing attention being given to drug utilization review (DUR) as a technique for evaluating effectiveness, costs and quality of drug prescribing and drug utilization, as well as a method of promoting cost-effective drug therapy without sacrificing quality of care.

The literature is replete with articles and reports dealing with one or another aspect of DUR. Many of them are purely descriptive and, while reflecting the 'state of the art' on DUR, seem to lack the theoretical basis upon which an appropriate process could be widely established.

A fairly recent review article by Rucker (1983) of the College of Pharmacy at the University of Illinois not only provides an excellent survey of the current status of DUR programs, but also contains a comprehensive bibliography of the major contributions on this subject. Rucker discusses the conceptual factors which underlie the adoption of a DUR system, variations in types and levels of review, reasonable objectives for the operation of a DUR program, the administrative procedures involved in the program's operation, the standards embodied in the process, as well as a discussion of other possible interventions for the purpose of promoting and attaining more rational drug therapy. There also is a section on issues involving cost effectiveness of drug therapy (meaning that expenditures should be incurred to improve patient health status as long a the cost is less than or equal to the benefits), and a section on the limitations of the DUR model. In this later section, some of the issues raised were: the position that a DUR committee might adopt in evaluating the use of placebo therapy; the need for uniform data elements; the reliability of diagnostic information; the methods available to ensure the confidentiality of patient records; practitioner 'regression' after initial stimulus from DUR; shared professional jurisdiction covering both practice and DUR implementation; a financing mechanism to ensure continuity of the DUR function; potential catalysts that might be enlisted to support the DUR concept; and the status of patients not covered by a DUR program.

In contemplating the future of DUR developments in the United States, for which there is a very close parallel to the situation in

Canada, Rucker says:

> Can DUR be regarded as a workable option for improving the use of prescription medication? On the one hand, if the index for prognosis is measured by the number of mature operating units, the number of investigators who have accumulated significant knowledge about the subject, the political climate, or professional enthusiasm for the concept, then a pessimistic conclusion seems inescapable.
>
> On the other hand, if the index is based upon documented shortcomings in drug-use practices, the feasibility of developing and applying standards of care, the possibility of focusing remedial efforts on a minority of clinicians, or the underlying pressures militating toward social progress, then a more optimistic argument may be tenable.
>
> Regardless of how these conflicting forces evolve, practitioners should contemplate that prescribed drugs represent the single therapy ordered most frequently in medical practice today and that some form of validation of its appropriateness is inevitable as technical and non-technical knowledge about prescribing increase.

8.3.3 Use of Educational Techniques

The review of the literature on this topic considered the educational process at the undergraduate medical level, the post-graduate medical level, and the activities subsumed under the title 'continuing medical education' (CME).

Several problems are apparent with respect to undergraduate medical education and pharmacology, including: a) lack of vertical and horizontal integration - pharmacologic teaching is scattered across all years and subjects; b) excessive emphasis on lectures; c) lack of structured and problem-based opportunities for students to acquire and practice the problem solving, decision-making and integration which will characterize their post-graduate lives; d) lack of structured active learning; e) lack of early clinical exposure to clinical problems in the context of basic science to permit application and generalization; and f) lack of innovation in medical education in pharmacology.

There is an urgent need to support projects that will remedy these problems.

The review identified very few studies which provided a solid foundation for the development of educational policies directed to improving prescribing abilities of physicians. However, the review indicates that sustainable effects on drug prescribing can be achieved by designing interventions that: a) are based on patterns of prescription by practicing physicians; b) target users/heavy prescribers; c) focus on specific drugs associated with problems of improving quality of care (e.g. antibiotics); d) make use of special educational materials for the intervention (e.g. unadvertising employing behavioural principles); e) incorporate individual feedback on drug pattern, and identify possible problem areas; and f) include individual verbal counselling or meetings about drug use.

Conversely, sustainable effects on drug prescribing are not achieved by: drug bulletins, public awareness campaigns, lectures, seminars, videos, cassette audio tapes, price lists, reminder notes or checklists, decision-making algorithms, handbooks, guidelines, focussing on cost as an issue, mailed brochures and "unadvertising" alone.

In addition there is a the need to design and conduct solid methodological studies to answer such questions as:

a) Do interventions work better on poor prescribers?

b) Can repeating the intervention with non-responders at a reasonable interval (e.g. 3 months) improve impact?

c) Can we generalize these examples to other prescribers?

d) What is the minimal audit, intervention or feedback package necessary for accurate predictions?

e) Are the results different depending on medical subspecialty?

f) Is there a difference in the quality of prescribing between post-graduate trainees and practicing physicians?

g) Is there a difference in quality of prescribing between Foreign Medical Graduates (FMGs) and Canadian graduates?

h) Have any educational interventions proven to be cost-effective?

i) Are there differences in the effectiveness of educational maneuvers between teaching hospitals and non-teaching hospitals?

8.3.4 Introduction of Innovative Payment Strategies

The most frequently discussed alternative method of payment is that of a capitation approach whereby the pharmacist would be paid a fixed sum for each person on his/her list which would cover the costs of all prescriptions needed by those for whom the capitation payment has been made.

Canada has had very little experience with the use of a capitation system. It has been used for many years in The Netherlands and in some cases, generally in isolated rural areas, under the National Health Service in the United Kingdom. Perhaps where capitation has been most widely used is by Health Maintenance Organizations (HMOs) in the United States. The evidence is that a capitation payment provides a strong incentive for pharmacists to dispense the least expensive product meeting the prescriber's specifications. Moreover, when the capitation method of payment was applied to independent pharmacists not involved in HMOs, not only was there a selection of the least expensive drug product which could be dispensed safely, but there was also a substitution of non-prescription drugs for prescription ones, when the former would be equally effective.

There is little question that capitation reimbursement is bound to increase, even over the short-term. Even from the moderate testing that has been done to date on these capitation experiments, the results have shown that they have been successful. When prescribers have been included within the capitation arrangements the results have proven to be even more successful in controlling costs without having a negative impact on quality of care.

At the same time there has been increased attention to alternative methods for reimbursement to pharmacists for prescriptions dispensed under both public and private drug benefit programs. Interest has been generated in developing new ways of estimating acquisition costs, and attempts at using wholesaler estimated acquisition costs (WEAC) or manufacturer estimated acquisition costs (MEAC) have been implemented. There are modifications of the practice of utilizing average wholesale prices (AWP) like utilizing a percentage discount of the published AWP in order to force pharmacists to purchase drugs directly from the manufacturer.

There continues to be interest in the application of maximum allowable costs which is a variation of the Prescriptions at Reasonable Costs (PARCOST) schedule utilized in Ontario. A new variation of the Maximum Allowable Cost (MAC) program is the Pharmacy Incentive Plan (PIP) which reimburses pharmacists at a percentage (initially suggested at 150%) of the lowest cost generic's published AWP. The PIP has not been implemented as yet but is expected to be introduced in the near future.

Another innovative suggestion that has been presented from time to time is to develop a mail order pharmaceutical service, particularly for medications for chronic conditions for which there is ample lead time for dispensing the medication, particularly in the case of prescription refills. Experience with mail-order systems has demonstrated the potential for savings in such an arrangement and the practice is increasing, albeit slowly, particularly in the United States.

Other new directions which have been introduced into the prescription drug system of various countries, and to some extent in

Canada, include: a) the use of pharmacy buying cooperatives, or group purchasing, in an attempt by independent pharmacists to achieve economies by collectively buying in greater quantities; and b) the formation of Preferred Provider Organizations (PPOs) of pharmacies, which contract to provide specified benefits to a group of identified recipients on the basis of a pre-agreed, and usually discounted, schedule of fees.

8.3.5 Alternative Health Care Delivery Systems

The most talked about, and fastest spreading, alternative health care delivery system, primarily in the United States but now being promoted also in the United Kingdom and even in Canada, is the Health Maintenance Organization (HMO).

Reports from the United States have indicated the high degree of acceptance of HMOs, particularly over the last decade. Enrollment in HMOs has increased significantly since the mid-1970s and now stands at close to 20 million enrollees. During 1984 the enrollment increased by more than 20% and it is projected that HMO enrollment will increase to over 50 million by the early 1990s.

The significance of this for drug utilization and drug costs is that HMOs have proven to be cost effective in many aspects of their delivery system. The incentives incorporated in this alternative delivery system, of capitation payment rather than fee-for-service, extend beyond the more efficient use of in-patient hospital services, more appropriate use of physician services, and the encouragement of preventive health measures in hopes of decreasing the severity and number of illnesses that require extensive resources and hospitalization, to areas such as the more appropriate prescribing of drugs and the dispensing of less costly products. HMOs have demonstrated that a substantial reduction in the cost of prescription (and very often non-prescription) drugs to members can be achieved through the use of closed formularies, encouragement to substitute lower cost generically equivalent products, direct purchase of drugs in large quantities, use of competitive bidding, use of advanced computer programs to identify aberrant patterns of prescribing or utilization, and a sophisticated program of drug utilization review. It has been estimated that prescription drug costs in an HMO are about half of those in community pharmacies.

8.3.6 Encouragement of Generic Substitution

During the 1960s there was widespread fear that inferior counterfeit drugs were being substituted for genuine brand-name products. As a result, legislators in most industrialized countries adopted laws which made it illegal to substitute any product for the brand identified in the prescription unless prior approval was obtained from the prescribing physician. Consequently, throughout most of the 1950s and 1960s there was almost universal acceptance of the practice of dispensing the precise brand-name product identified in the prescription.

Beginning in the late 1960s, however, there began to be questioning of the wisdom of a policy which restricted the opportunity for pharmacists to exercise their professional judgement in the selection of products to fill prescriptions. After all, pharmacists had the right, in fact responsibility, to select the appropriate product when filling a generically written prescription. Why shouldn't the same right be extended to brand-name prescriptions, unless the prescriber specifically indicated otherwise. By the middle and late 1960s a substantial proportion of prescriptions were being written generically and at the same time the reputation of numerous manufacturing firms became firmly established and standards and restrictions were imposed on all products, including imports, which raised the confidence that available products met standards of efficacy and reliability. During that same period, there were also growing complaints about the high prices of prescription drugs resulting from the near exclusion monopoly in several drug entity markets.

As a result there began a reversal of positions on the anti-substitution laws by many professionals as well as consumers, and particularly by organizations representing their interests. Starting in the early 1960s, there began a repeal of the various anti-substitution laws throughout Canada and the United States. By the early 1980s all of the anti-substitution laws had been repealed. Ontario passed legislation in 1972 (Bill 144) allowing pharmacists to select the appropriate product to dispense in filling a prescription, provided that: a) the product chosen was listed in the PARCOST CDI, and b) the prescribing physician had not specifically forbidden drug product substitution. The Ontario law is very similar to other provincial laws throughout Canada and comparable to those adopted in the U.S.

In general, although having a variety of specific provisions, the repeal of the anti-substitution laws has meant that pharmacists are allowed, and in some cases required, to dispense a lower cost, but generically equivalent, product than the one specifically identified in the prescription. The evidence is clear that substantial savings (20%-25%) occur when drug substitution is practised and that the incidence of generic substitution, while increasing at a very slow pace, is becoming an accepted fact of life. It has been noted by a well-known observer of the American scene that: "There is a growing realization that the great generic controversy is essentially over... the major struggle seems to be over, and the proponents of generics have won. The future will probably see merely mopping-up actions."

The opportunity for generic substitution is substantially greater in Canada than in the United States. This is because in 1969 Canada amended its Patent Act, Trade Marks Act, and Food and Drugs Act to provide for compulsory licensing to import patented pharmaceuticals. Each applicant, unless disapproved by the Commissioner of Patents, could obtain a license to import pharmaceuticals and market them in competition with the originator's brand-name product. This means that all drug entities in Canada are open to the opportunity for multi-product availability. Thus, the potential for drug product substitution is greater in Canada than in any other country.

The recent report by the Eastman Commission of Inquiry on the Pharmaceutical Industry (Eastman, 1985) contained some very interesting observations about the consequences of generic substitution in Canada. It said, for example, that:

> The generic firms have introduced an element of vigorous competition in the market for pharmaceutical products in Canada. ... In 1983, the prices of generic drugs were 51% of the prices of the patent-holding firms for substitutable brands. The consequences of compulsory licensing is that Canadian consumers and taxpayers paid $211 million less in 1983 than they would have for the same drugs in its absence.

8.3.7 Need for an Effective Data Linkage System

To be effective most of the suggested possible solutions to the problems of drug utilization in Canada are dependent upon the availability of reliable and comprehensive data. These data are needed both in terms of providing the basis for sound managerial decisions as well as to evaluate the extent of rational drug prescribing by the medical profession. Drug utilization review, educational strategies, and the evaluation of any proposed interventions meant to influence prescribing dispensing and patient consumption patterns cannot take place without the data to support those efforts.

Thus, there is the need to develop and implement a Management Information System (MIS) as well as a computerized system for recording and linking information about prescribing, dispensing and utilization patterns. Such a system must allow for: a) linking information about who prescribes what drugs, in what amounts and for what duration; b) patterns of what products are used to fill these prescriptions; and c) the behaviour of patients in compliance with drug regimens. There is evidence that 'explicit' systems which directly link the clinical diagnosis with the drug, dosage and duration of therapy are more effective than 'implicit' systems which associate independently generated diagnostic and therapeutic data bases. Also, collecting and processing accurate and uniform cost accounting data will enable the system of drug distribution not only to determine accurate estimates of operating costs upon which to construct reasonable dispensing fees, but also to know more precisely the various components of pharmacy operations such as cash flow, inventory levels, accounts receivable, and other similarly important items. Without all these different types of data and the creation of an appropriate and comprehensive information system to handle them, the system is seriously handicapped in identifying deficiencies and where to apply corrective measures.

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